

MUTAGENIC EFFECTS OF
SODIUM SACCHARIN (FDA No. 71-11)

Complaint Report No. 6

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STUDY OF MUTAGENIC EFFECTS OF
SODIUM SACCHARIN (FDA No. 71-11)

Prepared for:

Department of Health, Education and Welfare
Public Health Service
Food and Drug Administration
5600 Fishers Lane, Room 4C-25
Rockville, Maryland

Contract No. FDA 73-215
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Submitted by: G. W. Newell, T. A. Jorgenson, V. F. Simmon

Approved:

W. A. Skinner

W. A. Skinner, Executive Director
Life Sciences Division

INTRODUCTION

Under contract to the Food and Drug Administration, SRI is examining the mutagenicity of selected chemical compounds (Contract No. FDA 73-215). This report describes the results of tests conducted on sodium saccharin (FDA No. 71-11). It presents detailed descriptions of the methodologies used to perform these tests.

Four methods were used for evaluating the genetic hazards of the test compounds. These were: (1) host-mediated assay, (2) in vitro microbial assay, (3) dominant lethal test, and (4) mouse translocation test. Each procedure is described in detail below.

For the compound under consideration in this report, single and repeated oral administrations were performed at three concentrations for both the host-mediated assay and the dominant lethal test. The amounts were: (1) a maximum level--the calculated LD₅ or 5 g/kg (whichever was lower); (2) an intermediate level--1/10 of the LD₅ or 1 g/kg (whichever was lower); and, (3) a low level--1/100 of the LD₅ or 200 mg/kg (whichever was lower). For sodium saccharin the maximum level was 5 g/kg, the intermediate level 1 g/kg, and the low level 200 mg/kg.

In the mouse translocation test the test material was fed in the diet at two dosage levels. These were: a high level--the calculated LD₅ or 5 g/kg, whichever was lower, and a low level--1/10 of the LD₅ or, in the case where 5 g/kg was used, 1 g/kg. For sodium saccharin the high level was 5,000 ppm, and the low level was 1,000 ppm.

SUMMARY

Host-Mediated Assay - Mouse

Sodium saccharin (FDA No. 71-11) was not mutagenic in the host using Salmonella typhimurium TA1530, nor did it increase the mitotic recombination frequency in the host-mediated Saccharomyces cerevisiae D3.

In vitro Assay

In the in vitro assays, sodium saccharin was not mutagenic to S. typhimurium strains TA1530, TA1535, TA1536, TA1537, and TA1538, either in the presence or absence of metabolic activation. At a concentration of 5%, sodium saccharin did not increase the mitotic recombination frequency of S. cerevisiae D3.

Dominant Lethal Test - Rat

This experimental procedure produced no consistent responses to suggest that sodium saccharin (FDA No. 71-11) is mutagenic to the rat. The positive reference compound, TEM, a known mutagen, generally produced mutagenic responses from the first through the fifth weeks of the experiment, as expected. Mathematical treatment of the dominant lethal data, conducted according to a statistical program outlined by FDA, failed to show consistent significant differences (that could be attributed to an effect of sodium saccharin) at $P < 0.01$ or $P < 0.05$.

Translocation Test - Mouse

An extensive translocation study of sodium saccharin (FDA No. 71-11) was conducted in mice to investigate whether heritable mutagenic events occur when the compound is repeatedly ingested over an extended period.

Sodium saccharin was administered in the diet for seven weeks at two concentrations (1,000 and 5,000 ppm), eighty adult male mice per group. A group of forty control mice received the diet only during this

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Sodium saccharin was administered in the diet for seven weeks at two concentrations (1,000 and 5,000 ppm), eighty adult male mice per group. A group of forty control mice received the diet only during this

time, while a positive control group received triethylenemelamine (TEM) for four weeks in the drinking water. Each male was bred to two virgin females to produce an F₁ generation, the males of which were raised to maturity. One hundred F₁ males in the control and TEM groups and 200 F₁ males per sodium saccharin treatment level were bred to three virgin females. Evaluation of the pregnant females provided data that identified the nonbreeders, presumptive steriles, and partially steriles in each treatment group. Rebreeding these suspect animals reduced the number to three control, 20 TEM, and five sodium saccharin-treated males (three 1,000 ppm and two 5,000 ppm). Three controls, three TEM, and two sodium saccharin (1,000 ppm) F₁ males were subjected to cytogenetic testes evaluation of meiotic cell preparations. None of the control meiotic chromosomes showed heritable cytogenetic abnormalities, while all three TEM males each had single reciprocal translocations. One of the two sodium saccharin (1,000 ppm) males (F₁ 1343) was normal while the other male (F₁ 1389) had a single reciprocal translocation.

HOST-MEDIATED ASSAY - MOUSE

Background

The host-mediated assay combines the advantages of the mammalian metabolic system with those of microbial systems for detecting mutagens or metabolites of chemicals that are not mutagenic. Microbial assays allow both the exposure of large cell populations to the chemical being tested and the determination of mutation frequencies. In addition, microbial assays are relatively inexpensive compared with other systems of detecting carcinogens. The mammalian organisms provide the metabolic activities present in mammals that are absent in microorganisms. For example, dimethylnitrosamine is not mutagenic on direct exposure to bacteria but is mutagenic in the host-mediated assay.

In the host-mediated assay, the indicator microorganism is injected into the host's peritoneal cavity at the same time the host receives the test compound by some other route, such as oral intubation or intramuscular injection. The microorganism is allowed to incubate while the animal metabolizes the compound. After the organism has had a chance to incubate, it is removed from the animal and assayed for mutations. Theoretically, during the incubation period, the organism is then exposed to whatever metabolite normally might reach the various tissues in the animal. By comparing the mutagenicity of the compound in vitro with that obtained in the host-mediated assay, it is possible to determine if any activation or deactivation of the test compound has occurred during metabolism in the animal. For this report, a detailed description of the methodology has been provided even though it has been generally outlined in the literature (e.g., E. Zeiger and D. Brusick. The host-mediated assay--a protocol for Salmonella and Saccharomyces. Newsletter of the Environmental Mutagen Society 5, 32-34, 1971).

Materials and Methods

Microorganisms

A histidine auxotroph of Salmonella typhimurium TA1530 was used in these studies to measure biochemical reversion mutations. The yeast Saccharomyces cerevisiae D3 which is a diploid organism heterozygous for two linked genes (ade2 and his8), was used to measure for mitotic recombination.

Animals

Male Swiss albino mice, weighing an average of 28-30 g, were used for this study and maintained on a diet of Purina Lab Chow. The mice were obtained from Simonsen Laboratories, Gilroy, California.

Preparation of Microorganisms for Inoculation

The Salmonella strains were maintained on tryptone-yeast extract agar slants. To prepare the organism for inoculation into mice, a small inoculum from an agar slant was added to a broth consisting of 1.0% tryptone and 0.5% yeast extract. This culture was incubated for 24 hr at 37°C. The resulting suspension of cells was then adjusted to a concentration of $3-5 \times 10^8$ viable cells/ml using a spectrophotometer.

The yeast strain was maintained on yeast extract (0.5%) glucose (5.0%) agar slants. To prepare the yeast for inoculation into mice, a small inoculum from the agar slant was added to a broth consisting of 5% glucose, 0.5% yeast extract, and 0.2% peptone. This culture was incubated on a rotary shaker at 30°C for 24 hr. The cell concentration was adjusted spectrophotometrically to a concentration of $1-3 \times 10^8$ viable cells/ml before inoculating the animals.

Inoculation of the Mice

Two ml of the appropriate organism was inoculated into the peritoneal cavities of the mice using a 23-gauge needle. The area of inoculation was washed with ethanol before injection. The test compound was administered simultaneously with the inoculation.

Administration of Test Compound

The test compounds were administered by oral intubation using an 18-gauge intubating needle. The compound was dissolved in water or suspended in Mazola pure corn oil to a concentration requiring a 0.4 ml volume for each intubation.

The positive control compound for Salmonella, dimethylnitrosamine (DMNA), was dissolved in 10% ethanol to a concentration that would provide a 30-g mouse with a dose of 100 mg/kg. The positive control for the yeast, ethyl methane sulfonate (EMS), was dissolved in sterile saline to give a dose of 350 mg/kg/mouse. Positive control compounds were administered in 0.10 ml volumes by intramuscular injection.

Negative controls were run in all experiments. The negative control consisted of administering the solvent used for the test compound by oral intubation.

Autopsy and Recovery of Organisms

All test groups were sacrificed 4 hr after inoculation of the organism and administration of the test compound. The mice were sacrificed by cervical dislocation, their exterior abdominal regions were washed with ethanol, and 2 ml of sterile saline were injected into the peritoneal cavity of each mouse. The peritoneal cavity was opened aseptically, and the exudate withdrawn using a tuberculin syringe without a needle. The peritoneal exudates from each mouse were treated individually. They were placed in sterile tubes and immediately put in an ice bath. All plating of the samples was begun immediately after removal from the mouse.

Enumeration of Total Viable and Mutant Cells

Tenfold serial dilutions were made for each peritoneal exudate by serially adding 0.5 ml of sample to 4.5 ml of sterile saline. For the bacteria, a concentration series from 10^0 to 10^{-7} was prepared and for the yeast a series from 10^0 to 10^{-5} .

To enumerate the total viable bacteria, the 10^{-6} and 10^{-7} dilutions were plated by adding 0.2 ml of sample/plate to 3 separate plates. Each sample was spread over the surface of the plate using a sterile, bent glass rod. The medium used to enumerate total viable cells was as follows:

Bacteria Complete Medium

Tryptone	1.0%
Yeast extract	0.5%
Agar	2.0%
Dist. H ₂ O	to desired volume

To enumerate the revertant mutant bacterial cells, the 10^0 (and the 10^{-1} dilution if a large number of revertants were expected) dilutions were plated as described for enumerating the total bacteria. Six plates were used for each sample. The medium used for enumerating mutants was as follows:

Bacteria Minimal Medium

(NH ₄) ₂ SO ₄	0.2%
K ₂ HPO ₄	1.4%
KH ₂ PO ₄	0.6%
Na citrate	0.1%
MgSO ₄	0.02%
Biotin	0.5 μ g/ml
Glucose	0.5%
Agar	2.5%
Dist. H ₂ O	to volume

The glucose and biotin were sterilized separately and added to the autoclaved salt solution.

All bacteria were incubated at 37°C, the bacteria complete plates for 18 hr, and the bacteria minimal for 40 hr. If the plates could not be counted at this time, they were refrigerated.

To enumerate the yeast (both total viable cells and mitotic recombinants), samples from the 10^{-2} to 10^{-5} dilutions were plated on a yeast complete medium. They were plated in the same manner as described for the enumeration of the total bacteria. Total viable counts were

usually obtained by counting the 10^{-5} or 10^{-4} plates. The number of mitotic recombinant colonies was usually obtained by scanning the 10^{-3} or 10^{-2} plates with a dissecting scope at 10 X. The mitotic recombinants were seen as either red colonies or as red sectors on a normally white yeast colony. The prominence of the mitotic recombinants was enhanced by refrigerating for several days following the normal incubation of the yeast at 30°C for 48 hr.

The medium used for plating yeast was as follows:

Yeast Complete Medium

Yeast extract	0.5%
Peptone	0.35%
Glucose	2.0%
Agar	2.5%
KH_2PO_4	0.15%
$\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$	0.05%
$(\text{NH}_4)_2\text{SO}_4$	0.45%
Dist. H_2O	to desired volume

Data Handling

The data from all mice were used unless a great deal of contamination occurred or low recovery rates were obtained, possibly because the organism might have been injected into some organ rather than the peritoneal cavity. The number of colony forming units (CFU) or mitotic recombinants was determined by:

$$\frac{\text{No. CFU/plate}}{\text{No. plates}} \times \frac{1}{0.2} \times \frac{1}{\text{dilution factor}} = \text{CFU/ml in undiluted exudate}$$

The mutation frequency (MF) was calculated by:

$$MF = \frac{\text{total mutant cells}}{\text{total population}}$$

Treatment Groups

All treatment groups, including the positive and negative controls, consisted of 10 mice. The method used to determine concentrations of test compound is described in the section on the dominant lethal test.

The following groups were tested for all three organisms:

<u>Group</u>	<u>Treatment</u>	<u>Day of Treatment on which Test Organism was Injected</u>
1	Maximum tolerated dose	1
2	Intermediate dose	1
3	Low dose	1
4	Appropriate positive control	1
5	Appropriate negative control	1
6	Maximum tolerated dose	5
7	Intermediate dose	5
8	Low dose	5
9	Appropriate negative control	5

For testing FDA No. 71-61, the following doses were used:

Maximum dose - 1400 mg/kg
Intermediate dose - 140 mg/kg
Low dose - 14 mg/kg

In vitro Tests

The method described by Ames was used to determine in vitro mutagenicity for the bacteria (B. N. Ames, W. E. Durston, E. Yamasaki, and F. D. Lee. Proc. Nat. Acad. Sci. U.S.A. 70, 2281-2285, 1973).

To determine the in vitro mitotic recombination frequency of the test compound on the yeast, it was first necessary to determine what level of the test compound gave a 50% survival of the organism after a 4-hr exposure at 30°C. If the compound showed no lethal effects, a concentration of 5.0% w/v was used. In the actual test for mitotic recombination, the yeast (approximately 5×10^7 cells/ml) was exposed to the appropriate concentration of compound for 4 hr, and then samples were plated as described for determining mitotic recombinants in the section on host-mediated assay. The mitotic recombination frequency is expressed as sectors per 10^5 survivors. This was compared with a negative control.

In the yeast in vitro studies, EMS was employed as the positive control. In the bacterial in vitro assays, 2-fluorenamine was employed as the positive control for metabolic activation.

Results and Discussion

Host-Mediated Assay

Table 1 summarizes the results of the host-mediated assay of sodium saccharin (FDA No. 71-11) with Salmonella typhimurium TA 1530. (The data for individual mice are presented in Tables 3 and 4.) In the single and five day treatment regimen, no mutagenic effect was observed when sodium saccharin was administered orally at doses of 0.2, 1.0, and 5.0 g/kg. The positive control DMNA was mutagenic when given as a single intramuscular injection at 0.1 g/kg. We conclude that sodium saccharin is not mutagenic to S. typhimurium strain TA1530 at the doses tested when given as a single or multiple oral treatment. The known mutagen DMNA significantly increased the reverse mutation frequency of TA1530.

Table 2 summarizes the result of the host-mediated assay with Saccharomyces cerevisiae D3. (The data for individual mice are presented in Tables 5 and 6.) In the first experiment of Table 5, many of the plates we received from our supplier were contaminated (this problem was reported in Technical Progress Report No. 1, October 12, 1973). As a result, data from only a few mice were obtained. Therefore the experiment was partially repeated. We conclude that based on the data from these two experiments, sodium saccharin did not increase the mitotic recombination frequency of S. cerevisiae D3 at the doses tested when given as a single or multiple oral treatment. The known mutagen EMS significantly increased the mitotic recombination frequency of S. cerevisiae D3.

In vitro Microbial Assay

In the in vitro assays, sodium saccharin was not mutagenic to S. typhimurium either in the presence or absence of the metabolic activation system (Table 7). At a concentration of 5% sodium saccharin, a twofold increase in the number of mitotic recombinants was observed (Table 8). In contrast, the known mutagen/carcinogen EMS increased the mitotic recombination frequency by 50-fold at a concentration of 1%.

DOMINANT LETHAL TEST - RAT

Background

Dominant lethal assays of compounds suspected of causing major genetic damage in animals have been carried out, for the most part, in mice. One exception was a comparative study by Bateman with mice and rats to evaluate the dominant lethal effect of triethylenemelamine (*Genet. Res. Camb.* 1, 381-392, 1960). Although there are cost savings in using the mouse rather than the rat, the latter has experimental advantages in providing more definitive information when attempting to assess the incidence of early fetal deaths. Also, corpora lutea counts in the mouse are difficult and relatively imprecise (S. S. Epstein and G. Rohrborn, *Nature* 230, 469-470, 1971). For this project, adult Sprague-Dawley-derived rats, from a closed random-bred colony, were used for the acute toxicity determinations as well as the dominant lethal assay.

In the mammalian test procedure, the compound under investigation was administered orally either once or on five successive days to proven male breeders. Following dosing, each male was mated with two adult female rats for seven days. The females were then removed, and new females again were added for another week of breeding. This sequence continued for eight weeks. Thus, the procedure is designed to indicate possible mutagenic effects on the male sperm, with the normal female acting as a carrier to demonstrate abnormalities that may have occurred in the male. Effects were evaluated by examining the state of fetal development during the middle to latter stages of gestation.

The experimental approach is presented below in a step-by-step manner to ensure clarity and an understanding of the preciseness of procedures used in this phase of the program.

Materials and Methods

Animals

Adult male and female Sprague-Dawley-derived rats were supplied by Simonsen Laboratories, Gilroy, California. The males were proven breeders, while the females were of virgin stock. Purina Lab Chow and water were available at all times.

Chemical Supply

All compounds or natural materials were supplied by the Food and Drug Administration. Each compound or natural material was provided in a ready-to-use form and was identified by both name and FDA code number. Sufficient quantities to complete all aspects of the experimental program were received. Excess supplies were placed in storage, should they be needed for future reference.

Solubility Studies

Solubility of each compound or natural material was investigated using such agents as water, propylene glycol, polyethylene glycol, corn oil, tricaprylin, carboxymethylcellulose, or methylcellulose (Methocel) to determine the most appropriate vehicle for administration. Because of the low toxicity of most materials and the consequent high dosages required, many of the test materials were administered as suspensions.

Acute Toxicity (Single and Multiple Dose)

Although acute toxicity information on some of the compounds was available in the literature, confirmatory tests were done to obtain an LD₅₀ under our laboratory conditions and for this strain of rat. If no data were available, a broad, range-finding dose regimen was conducted, followed by an accurate determination of the oral LD₅₀.

A range-finding dose regimen was conducted using the acute data to determine an accurate multiple dose LD₅₀. Nonstarved animals were used throughout this part of the study because of the multiple dosing regimen.

Dosage Selection

In selecting the three dosage levels for the experimental study, two approaches were used:

- (1) If a finite LD₅₀ was obtained, the highest dose level was the calculated LD₅. The intermediate dose was 1/10 of the calculated LD₅, and the lowest dose was 1/100 of the calculated LD₅.
- (2) If the LD₅₀ was greater than 10 g/kg (a mutually agreed on upper limit), the highest dose was 5 g/kg; the lowest dose was 200 mg/kg; and the intermediate dose was 1 g/kg. These guidelines were used for both single and multiple dose experimental study groups.

Control Groups (Vehicle and Positive)

A vehicle control group (corn oil, water, Methocel, etc.) was included in each experimental study. Vehicle control animals were included in both the acute and subacute studies. In this manner, breeding and implant data were obtained for each vehicle control and were used as reference comparisons for the experimentally treated animals, both the single and multiple treatment groups. The positive reference control was the known mutagen, triethylenemelamine (TEM), given at a dose of 0.2 mg/kg as a single i.p. injection. Breeding and implant data were obtained for eight weeks.

Acute Studies (Single Dose)

In an acute study, ten experienced breeder male rats per treatment group were administered a single oral dose of test compound. Controls were treated as previously described. Within two or three hours of dosing, each male was presented with two virgins of breeding age for a period of seven days. Females were replaced weekly over a total mating period of eight weeks.

Subacute Studies (Multiple Dose)

For the subacute assay, the experimental parameters used in the acute test were employed, with three exceptions: (1) five dosings

were given at 24-hour intervals; (2) weekly mating periods lasted for seven rather than eight weeks; and (3) the same positive control group used for the acute dosing also served as the reference group for the subacute assay.

Necropsy

Starting two weeks after the first day of breeding, one-fourth of the pregnant females in each group were sacrificed on four successive days. This schedule allowed for sacrifice of females between 11 and 18 days of pregnancy. A complete autopsy of each female was done to determine if there was intercurrent infection, since such a condition can induce preimplantation loss and early fetal deaths (G. Rhorborn, *Humangenetik* 6, 345, 1968).

Observations

At time of sacrifice, each female was scored for early fetal deaths, late fetal deaths, living fetuses (all of which provide a total implant score), corpora lutea, and pre-implantation loss (determined by subtracting the total implant score from the total corpora lutea score).

Evaluation

The following parameters indicate effects in dominant lethal studies: total implants (live fetuses plus early and late fetal deaths), total dead (early and late fetal deaths), dead implants per total implants, and pre-implantation loss (calculated as the difference between the total corpora lutea and total implant counts). We also evaluated total corpora lutea because a significant change of this parameter could influence the significance of the pre-implantation loss. Total implants, total dead, total corpora lutea, and pre-implantation loss parameters were analyzed for significance by the t-test.

The index of dead implants per total implants was analyzed statistically by the t-test on arcsine (or angular) transformed data, as described in Experimental Design (Theory and Application),

by Walter T. Federer, The Macmillan Company, 1955. This index was computed for each female.

The assumptions underlying the analysis of variance and the usual tests of significance are discussed by C. Eisenhart (*Biometrics* 3, 1-21, 1947); W. G. Cochran (*Biometrics* 3, 22-38, 1947) discusses the consequences when the assumptions underlying the analysis of variance are not fulfilled. These two papers, plus one by Bartlett (*The use of transformations. Biometrics* 3, 39-52 and 96, 1947), provide background information on this subject.

Results and Discussion

Single and multiple dose toxicity data are presented below.

Oral Toxicity - Rat and Mouse

Compound: Sodium saccharin
FDA No.: 71-11

	Rat	Mouse
Single dose ^a	8.6 g/kg	11.6 g/kg
Multiple dose ^b	> 5 g/kg	> 5 g/kg

^aTen male, Sprague-Dawley rats, weighing 283-366 grams each, and ten male, Swiss Webster mice, weighing 19-27 grams each, were fasted overnight and then administered orally specified amounts of the candidate compound dissolved or suspended in water.

^bTen male, nonfasted Sprague-Dawley rats, weighing 263-351 grams each, and five male, nonfasted Swiss Webster mice, weighing 21-24 grams each, were administered orally specified amounts of the candidate compound dissolved or suspended in water.

After an evaluation of the toxicity data, dosage levels for the mutagenesis assays were selected as follows:

Single dose--5 g/kg, 1 g/kg, and 200 mg/kg

Multiple dose--5 g/kg, 1 g/kg, and 200 mg/kg

Throughout the experiment, the biological criteria used to evaluate mutagenic effects in the rat showed no consistent responses that could be attributed to treatment. There were occasional statistical differences between control and sodium-saccharin-dosed groups, but they were random and did not suggest a time or dose-response effect.

Table 9 presents summary data on the implantations per pregnant female, Table 10 summarizes dead implants per pregnant female, Table 11 summarizes dead implants per total implants, Table 12 summarizes corpora lutea per pregnant female, and Table 13 summarizes pre-implantation loss per pregnant female.

Appendix A presents a description of the statistical analysis procedures used for dominant lethal tests with an explanation of the computer printouts.

Appendix B contains computer printouts of the raw data and the statistical analyses.

Careful review and statistical evaluation of the data do not show sodium saccharin (FDA No. 71-11) to be a mutagen in the rat by the dominant lethal test.

HERITABLE TRANSLOCATION TEST - MOUSE

Background

Human populations frequently are exposed to man-made chemicals for extended periods, and often at borderline detectable levels. To evaluate the genetic hazards of such chemicals, it is considered prudent that such materials be studied in mammalian systems at several dosages in order to maximize detection of a mutagenic response.

Chemical induction of chromosomal aberrations in the mouse is an important experimental tool, in view of the many human genetic defects that are due to various chromosomal anomalies. To date, evaluations of chemically induced chromosomal aberrations have been attempted with the dominant-lethal test and cytogenetic studies of somatic and germinal cells of certain mammals. Although these test procedures can provide useful information, they do not measure heritable genetic effects. Obviously, the most important mutagenic effects are permanent and transmissible. A need has existed, therefore, for a method which can reliably identify compounds that cause heritable chromosomal aberrations in mammalian systems. The mouse translocation procedure would appear to be such a system.

A well-defined translocation test will determine the fertility of an F_1 male population derived from F_0 males treated with a test agent. Confirmation of a sterile or a partially sterile response can be obtained by cytological examination of the germ cells from suspected males. Sterility and partial sterility are closely correlated with the induction of translocation heterozygotes.

The procedure used in conducting this translocation test was based on experimental techniques described by Leonard and DeKnudt (Mutation Research 9, 127, 1970), Cattanach et al (Mutation Research 6, 297, 1968), Falconer et al (J. Genetics 51, 81, 1952), and Generoso (Meeting Environmental Mutagen Society, March 1971, p. 9, Abstracts); modifications of approach were made by staff of this laboratory in consultation with staff of the Genetic Toxicology Branch, Bureau of Foods, FDA.

Materials and Methods

Animals

Adult male and female ICR/SIM mice were supplied by Simonsen Laboratories, Gilroy, California. The F₀ males, used in the test compound treatment groups, were three- to four-month-old proven breeders. Females, used in the breeding phases, were 9- to 10-week old virgins.

Chemical Supply

All materials for evaluation were supplied by the Food and Drug Administration with the exception of N-methyl-N'-nitro-N-nitroso-guanadine (MNNG), which was purchased by SRI from Aldrich Chemical Co., San Leandro, California. Sufficient quantities to complete all aspects of the experimental program were received. Excess supplies have been placed in storage, should they be needed for future reference.

Acute Toxicity (LD₅₀)

Although acute toxicity information on some of the compounds was available in the literature, confirmatory tests were conducted to obtain an LD₅₀ under our laboratory conditions and for this strain of mouse. If no data were available, a broad, range-finding dose regimen was conducted, followed by an accurate determination of the oral LD₅₀.

Dosage Selection

Two treatment levels were used in the translocation test. In selecting these levels, two approaches were used:

- (1) If a finite LD₅₀ response was obtained, the maximum dose was the calculated LD₅; the lower dose was 1/10 of the calculated LD₅.
- (2) If the LD₅₀ was greater than 10 g/kg (a mutually agreed-upon upper limit), the maximum dose was 5 g/kg; the lower dose was 1 g/kg.

Reference Control

Two reference control groups were included in this contract program. One was run at the beginning of the series of translocation tests; the other was done at the end of the test series. In this manner, breeding and implant data were obtained at two separate time periods, as well as providing an increased reference-control data base. F_0 males in these groups were fed a finely ground commercial laboratory diet with corn oil added at a level of 2%; thereafter, all animals in these groups were fed a commercial pelleted diet. Water was available ad libitum. Control groups were treated in the same manner as compound test groups.

Positive Control

A positive control was run concurrently with a negative control.

For this group, the known mutagen triethylenemelamine (TEM) was administered initially in the drinking water (0.32 mg/l) for four weeks, at an approximate ingestion dose of 0.062 mg/kg/day. Fresh TEM solutions were prepared daily. A commercial pelleted diet was available at all times.

In this exploratory study, forty treated males bred to 81 females produced only 11 litters. The large number of sterile males and the small size of the litters showed that the dosage level was too high to allow production of sufficient numbers of offspring for adequate evaluation. A confirmatory TEM study using the same dosage regimen had been underway for two weeks when the first TEM data became available. TEM concentration was immediately reduced for the final two weeks to 0.124 mg/l, an intake level of approximately 0.024 mg/kg/day. Discussion of the results for both TEM experiments is presented in Results and Discussion.

Administration of Test Compounds

The candidate compound was fed in the diet to adult male mice for seven weeks. An appropriate amount of compound initially was dissolved or suspended in corn oil; then the compound-oil concentrate

was added at a level of 2% to a finely ground commercial diet of known composition. The use of corn oil assured even distribution of the compound and presented stratification of the test material in an otherwise dry diet. Diets prepared at two-week intervals were refrigerated at 4°C until fed to the animals. In addition, the diet was replaced in the feed containers every other day to minimize the possibility of compound loss.

Genetic Tests

After seven weeks of dietary compound treatment or four weeks of TEM drinking-water treatment, approximately 80 compound and 40 control treated males per group were mated with two adult virgin females each; after two weeks, each female was housed individually and allowed to litter. Impregnation time was based upon the date of parturition. Litters from the second week of breeding were discarded. Weanling females were discarded while males were raised to maturity (10-12 weeks). At maturity, 100 F₁ males per group for control groups and 200 F₁ males per group for compound treated animals were randomly selected and housed individually. Three adult virgin females were bred to each F₁ male for a period of two weeks; examinations were made daily for the presence of vaginal plugs. Females were sacrificed 14 days after mating; a uterine analysis was performed to determine the number of total, live, and dead implants.

Criteria for Classification of a Male as Sterile or Partially Sterile

An in-depth statistical review of breeding data from control animals was performed by Theodore W. Horner, Statistical Consultant, Division of Mathematics, Bureau of Foods, Food and Drug Administration. This review of a normal litter size distribution and discussions between the FDA and SRI technical staffs provided the necessary information for establishing the classification criteria for a male as sterile or partially sterile.

Classification of a F₁ male mouse as sterile or partially sterile was made according to the following criteria:

- "Partially Sterile" Male

- (1) If all three females are pregnant, each female must have 9 or fewer live implants---with at least one female having 6 or fewer live implants.
- (2) If two of three females are pregnant, both females must 9 or fewer live implants---with one female having 6 or fewer live implants.
- (3) If only one of three females is pregnant, this female must have 6 or fewer live implants.

- "Sterile" Male

- (1) None of three females pregnant---previously identified by presence of a vaginal plug.

Any F_1 male that did not fit one of the above-mentioned selection criteria was considered "normal".

F_1 males found to be sterile or partially sterile were held for future evaluation (i.e., additional breeding and/or cytogenetic study of meiotic chromosomes).

Evaluation

A careful review of the F_0 breeding and litter data was conducted to determine if there were possible correlations between compound treatment and breeding performance, litter size, or sex distribution.

F_1 males were identified as sterile or partially sterile by the evaluation method outlined above. Individual data were totaled to give the number of observed F_1 males (presumptive translocations) per treatment based on the breeding of 300-600 females per group. Various parameters were evaluated such as percent pregnancies, average litter size, average number of males per treatment bred to females with 0 - 5 or more dead implants, average number of females per treatment with 0 - 5 or more dead implants, percent per treatment with plugs, and percent pregnancies per treatment with and without plugs.

Meiotic Cell Cytogenetic Studies

Male mice that showed characteristics of presumptive translocation after two breedings were reviewed by FDA and SRI staff members. Selected males were then evaluated for chromosomal translocations by examination of meiotic preparations of the testes. Cytogenetic studies were conducted by Dr. K. S. Lavappa, Department of Cell Culture, American Type Culture Collection (ATCC), Rockville, Maryland.

The two testes from each animal were weighed and examined separately. Meiotic preparations were made with the air-drying technique. Spermatocytes in diakinesis-metaphase I were examined for the presence of translocations. From each testis, four slides were examined and 40 spermatocytes were scored per testis.

Results and Discussion

Acute Toxicity (LD₅₀)

The LD₅₀ in mice was 11.6 g/kg with 95% confidence limits of 10.5 to 12.8 g/kg. Based on the LD₅₀ data, the following dosage levels for the translocation study were selected:

Maximum dose	5,000 mg/kg
Minimum dose	1,000 mg/kg

F₀ Generation

Although information about the F₀ generation should be included in the evaluation of translocation data, often it has not been presented or discussed in the reporting of a translocation study. Information on breeding performance of the mouse strain used, litter size or distribution, sex distribution, and the effect of compound treatment on the above, can provide valuable background data.

Table 16 summarizes the breeding and litter performance of the F₀ generation. The TEM I experiment produced a high degree of sterility. Therefore, it was necessary to reduce the concentration of TEM in an ongoing second experiment. By reducing TEM in the drinking water to one-third the original concentration, the second experiment provided

us with a satisfactory mutagenic response. No adverse effects were observed in either of the sodium saccharin-treated groups. Both control groups performed in a normal manner for this strain of mouse.

Table 17 presents litter-size distribution of the F₀ generation mice. Although litter sizes were smaller in the TEM-treated groups, other groups had normal litter-size distributions.

F₁ Generation

Table 18 summarizes breeding data for the F₁ generation mice. In the TEM I experiment, there was a decrease in the percentage of pregnancies. Other groups responded normally for the ICR/SIM mouse strain.

Litter-size distributions are presented in Table 19. As was the case with the F₀ generation, TEM groups had smaller litters. Other groups were normal.

Dead implants per F₁ male are presented in Table 20; dead implants per female are summarized in Table 21. In both TEM studies and both sodium saccharin groups, there were greater numbers of females with 3 to 5 dead implants than in the control groups. Dead implant incidence for these latter groups was low and similar.

Table 22 presents a summary of the breeding results, by group, of those F₁ males found to be sterile or partially sterile. In Table 23, the individual F₁ animals are identified by number and treatment. TEM groups I and II showed an incidence of this response of 75% and 15%, respectively; the reference control and sodium saccharin groups had an incidence ranging from 1% to 2%. Females bred to partially sterile males in the TEM groups showed an increased number of dead implants along with a lesser number of viable implants. This condition was not seen in the reference control or sodium saccharin groups. Individual data on these animals can be found on the project "Translocation Data Sheets," which will be submitted separately to FDA.

Tables 24 to 26 present summary breeding and rebreeding data of presumptive F₁ males. In the first reference control experiment,

five males were nonbreeders and one met the criteria of "presumptive". When these animals were rebred, only two of these remained as nonbreeders. The second reference control experiment provided similar type responses. Out of 100 F₁ males in this group, six were found to be presumptive mutants after the first breeding schedule; the rebreeding of these males showed only one animal remaining as a presumptive. This male (No. 1455) had two females with seven viable implants per female and one female with plugs but no pregnancy; the rebreeding with three new females showed no evidence of mating (Table 24).

In Table 25, the effect of TEM producing heritable translocations is strongly implied. Eight F₁ males from the first TEM study produced six presumptive mutants by our evaluative criteria. Rebreading of these six a second and third time continued to show a presumptive mutant condition for all six animals. For the second TEM experiment with 112 F₁ males, 17 of these animals fit the criteria of "presumptive" after the first breeding schedule. When these 17 were rebred to new females, 14 of the males still remained as presumptive mutants.

For sodium saccharin (Table 26), 200 F₁ males (from the 1,000 ppm dietary treatment of the F₀ generation) showed ten animals to be presumptive mutants after the first breeding. When these ten were rebred, only three males still remained in the presumptive mutant category. For the 5,000 ppm sodium saccharin group, twelve males out of the 200 tested showed ~~no~~ evidence of presumptive mutancy after the first breeding. When the twelve were rebred, only two animals still remained in this category. One was a nonbreeder and the other a partially sterile.

Cytogenetic Studies

Table 27 shows the findings from the cytogenetic evaluation of meiotic cell preparations from those F₁ males selected by the FDA Project Officer for examination. Dr. Lavappa found the two control I, one control II, and one 1,000 ppm sodium saccharin mice to be cytogenetically normal. The three TEM I mice, however, each had single reciprocal translocations as did one sodium saccharin (1,000 ppm) male. His report to SRI included the following:

These animals were examined for heritable cytogenetic abnormalities (reciprocal translocations). Four of these animals, F₁ 103, 106, 108, and 1389 each had single reciprocal translocations. The other three animals, F₁ 15, 40, and 1455 were cytogenetically normal.

The original report by Dr. Lavappa and photographs are on file at Stanford Research Institute.

The main objective of this investigation was to study the methodology of performing mammalian translocation experiments and to evaluate such a procedure with a specific compound, sodium saccharin. The original experimental plan involved a single breeding of F₁ males to virgin females. The results of this effort produced relatively large numbers of nonbreeder and partially sterile animals, as many as four to eight per group. Examination of the breeding data from these suspect animals showed many not to have had evidence of mating--no evidence of a vaginal plug in any of the three females caged with a specific male. Thus, it was decided to rebreed each of these suspect males to three additional virgin females. Although this extra task went beyond the requirements of this contract, it was our intent that this procedure be developed in a manner which would provide maximum information, still considering the realistic output of effort and cost.

We believe this rebreeding of initial presumptive mutant males is a significant contribution to reducing the possible interpretive error of presumptive mutant occurrence. For definitive confirmation of these biological results, cytogenetic examination of these animals should be done. Cytogenetic study of meiotic cells is tedious and time consuming. If confirmation of presumptive males had been done after the first breeding schedule was completed, some 57 animals would have had to have been examined. After the rebreeding regimen, only 28 animals still remained as presumptive mutants. These totals include the TEM groups as well as the reference control and sodium saccharin groups. If the TEM animals are excluded, there would have been 34 presumptive mutants in the reference control and sodium saccharin group after the first

breeding; when rebred, only 8 animals remained as presumptive mutants (3 control, 3 in the 1,000 ppm group and 2 in the 5,000 ppm sodium saccharin groups).

Table 1
 SUMMARY OF HOST-MEDIATED ASSAYS WITH
SALMONELLA TYPHIMURIUM TA1530

Regimen	Compound	Dose/kg	Avg CFU per ml (X 10 ³)	Avg His ⁺ Revertants per ml	His ⁺ Revertants per 10 ⁸ CFU
Single Treatment	Negative Control		1.56	104	6.9
	DMNA	0.1 g	1.93	797	45.9
	Sodium saccharin	0.2 g	1.66	121	9.9
		1.0 g	1.95	87	4.5
		5.0 g	1.39	66	5.5
Multiple Treatment (5 doses)	Negative Control		1.06	80	8.8
	Sodium saccharin	0.2 g	0.88	66	6.6
		1.0 g	1.65	79	4.9
		5.0 g	1.32	75	6.4

Table 2
SUMMARY OF HOST-MEDIATED ASSAYS WITH
SACCHAROMYCES CEREVIAE D3

Regimen	Experiment No.	Compound	Dose/kg	Avg CFU per ml (X 10 ⁷)	Avg Ade ⁻ Recombinants per ml (X 10 ³)	Ade ⁻ Recombinants per 10 ⁸ CFU
Single Treatment	1	Negative Control		3.64	3.7	11.2
		EMS	0.35 g	3.48	28.6	96.8
		Sodium saccharin	0.2 g	2.48	2.4	12.2
			1.0 g	2.09	2.7	16.6
			5.0 g	1.05	1.7	15.3
2	2	Negative Control		2.69	2.0	5.8
		Sodium saccharin	1.0 g	1.81	1.4	8.1
			5.0 g	1.63	1.2	7.9
Multiple Treatment (5 doses)		Negative Control		2.69	2.0	5.8
			0.2 g	2.15	1.9	8.8
			1.0 g	1.82	1.6	7.4
			5.0 g	2.68	2.4	8.6

Table 3
HOST-MEDIATED ASSAY WITH SALMONELLA TYPHIMURIUM TA1530

The mice were given a single oral dose of sodium saccharin. The positive control, DMNA, was given intramuscularly.

Compound	Dose/kg	Mouse Number	CFU/ml (X 10 ⁶)	<u>His</u> ⁺ Revertants per ml	<u>His</u> ⁺ Revertants per 10 ⁶ CFU
Negative Control		1	2.60	113	4.3
		2	0.76	43	5.7
		3	1.73	109	6.3
		4	1.30	93	7.2
		5	1.48	109	7.4
		6	1.48	156	10.5
		Avg	1.56	104	6.9
DMNA (Positive Control)	0.1 g	1	1.67	625	37.4
		2	4.05	1230	30.4
		3	1.11	755	68.0
		4	2.25	450	20.0
		5	0.88	268	30.5
		6	1.32	940	71.2
		7	2.67	1130	42.3
		8	1.45	975	67.2
		Avg	1.93	797	45.9
Sodium saccharin	0.2 g	1	1.00	116	11.6
		2	1.37	160	11.7
		3	1.52	173	11.4
		4	0.62	90	14.5
		5	3.13	95	3.0
		6	2.98	68	2.3
		7	0.98	148	15.1
		Avg	1.66	121	9.9
	1.0 g	1	2.56	76	3.0
		2	2.73	93	3.4
		3	2.03	133	6.6
		4	2.00	85	4.3
		5	1.77	90	5.1
		6	1.06	46	4.3
		7	1.00	43	4.3
		8	2.48	127	5.1
		Avg	1.95	87	4.5

Table 3 (concluded)

HOST-MEDIATED ASSAY WITH SALMONELLA TYPHIMURIUM TA1530

The mice were given a single oral dose of sodium saccharin. The positive control, DMNA, was given intramuscularly.

Compound	Dose/kg	Mouse Number	CFU/ml (X 10 ³)	<u>His</u> ⁺ Revertants per ml	<u>His</u> ⁺ Revertants per 10 ³ CFU
Sodium saccharin	5.0 g	1	0.79	61	7.7
		2	1.87	53	2.9
		3	0.76	50	6.6
		4	0.57	47	8.2
		5	1.95	83	4.3
		6	1.70	83	4.9
		7	1.38	69	5.0
		8	2.12	84	4.0
Avg			1.39	66	5.5

Table 4
HOST-MEDIATED ASSAY WITH SALMONELLA TYPHIMURIUM TA1530

The mice were given sodium saccharin at the doses indicated for five consecutive days.

Compound	Dose/kg	Mouse Number	CFU/ml (X 10 ³)	<u>His</u> ⁺ Revertants per ml	<u>His</u> ⁺ Revertants per 10 ⁸ CFU
Negative Control		1	1.17	73	6.2
		2	1.85	82	4.4
		3	1.35	49	3.6
		4	0.35	49	14.0
		5	1.30	68	5.2
		6	1.02	83	8.1
		7	0.79	118	14.9
		8	0.82	86	10.5
		9	0.91	113	12.4
		Avg	1.06	80	8.8
Sodium saccharin	0.2 g	1	1.31	81	6.2
		2	0.11	5	4.5
		3	1.15	86	7.5
		4	1.35	34	2.5
		5	0.56	61	10.9
		6	1.35	69	5.1
		7	1.15	96	8.3
		8	1.12	86	7.7
		9	1.36	108	7.9
		10	0.68	36	5.3
		Avg	0.88	66	6.6
1.0 g		1	1.25	88	7.1
		2	2.18	51	2.3
		3	1.05	50	4.8
		4	1.52	64	4.2
		5	1.34	73	5.4
		6	1.39	73	5.3
		7	2.17	133	6.1
		8	2.27	96	4.2
		Avg	1.65	79	4.9
5.0 g		1	1.35	49	3.6
		2	1.26	62	4.9
		3	1.57	71	4.5
		4	1.23	73	5.9
		5	2.60	120	4.6
		6	1.00	53	5.3
		7	0.88	87	9.9
		8	0.65	83	12.8
		Avg	1.32	75	6.4

Table 5
HOST-MEDIATED ASSAY WITH SACCHAROMYCES CEREVIAE D3

The mice were given a single oral dose of sodium saccharin. The positive control, EMS, was given intramuscularly.

Experiment Number	Compound	Dose/kg	Mouse Number	CFU/ml (X 10 ⁷)	Ade ⁻ Recombinants per ml(X 10 ³)	Ade ⁻ Recombinants per 10 ⁶ CFU
1	Negative Control		1	3.53	2.0	5.7
			2	4.22	5.0	11.8
			3	3.00	3.5	11.7
			4	3.46	3.0	8.7
			5	6.61	6.5	9.8
			6	1.04	2.0	19.2
			Avg	3.64	3.7	11.2
	EMS (Positive Control)	0.35 g	1	4.55	23.5	52
			2	1.05	13.5	129
			3	5.77	58.5	101
			4	4.13	24.0	58
			5	3.17	17.0	54
			6	3.33	18.0	54
			7	5.22	61.5	118
			8	0.60	12.5	208
			Avg	3.48	28.6	96.8
	Sodium saccharin	0.2 g	1	0.45	1.0	22.2
			2	4.12	3.0	7.3
			3	3.03	1.0	3.3
			4	1.63	2.5	15.3
			5	1.82	3.0	16.5
			6	5.10	7.5	14.7
			7	0.24	0.5	20.8
			8	2.62	1.0	3.8
			9	3.31	2.0	6.0
			Avg	2.48	2.4	12.2
		1.0	1	1.83	6.0	32.8
			2	0.85	1.5	17.6
			3	0.29	0.5	17.2
			4	2.25	2.0	8.9
			5	5.22	3.5	6.7
			Avg	2.09	2.7	16.6
		5.0	1	1.67	2.5	15.0
			2	0.92	2.0	21.7
			3	0.55	0.5	9.1
			Avg	1.05	1.7	15.3

Table 5 (concluded)
 HOST-MEDIATED ASSAY WITH SACCHAROMYCES CEREVISIAE D3

The mice were given a single oral dose of sodium saccharin. The positive control, EMS, was given intramuscularly.

Experiment Number	Compound	Dose/kg	Mouse Number	CFU/ml (X 10 ⁷)	Ade ⁻ Recombinants per ml (X 10 ³)	Ade ⁻ Recombinants per 10 ⁶ CFU
2	Negative Control		1	5.28	4	7.6
			2	1.16	1	8.6
			3	3.20	3	9.4
			4	3.46	1	2.9
			5	2.57	3	1.2
			6	0.95	0	
			7	2.83	2	7.1
			8	2.03	2	9.9
			Avg	2.69	2.0	5.8
Sodium saccharin	1.0		1	2.12	2	9.4
			2	1.81	1	5.5
			3	1.05	2	19.0
			4	0.93	0	
			5	3.12	2	6.4
			Avg	1.81	1.4	8.1
5.0			1	1.11	1	9.0
			2	1.67	2	12.0
			3	2.33	1	4.3
			4	1.60	0	
			5	1.42	2	14.1
			Avg	1.63	1.2	7.9

Table 6
HOST-MEDIATED ASSAY WITH SACCHAROMYCES CEREVISIAE D3

The mice were given sodium saccharin at the doses indicated for five consecutive days.

Experiment Number	Compound	Dose/kg	Mouse Number	CFU/ml (X 10 ⁷)	<u>Ade</u> ⁻ Recombinants per ml(X 10 ³)	<u>Ade</u> ⁻ Recombinants per 10 ⁶ CFU
Negative Control			1	5.28	4	7.6
			2	1.16	1	8.6
			3	3.20	3	9.4
			4	3.46	1	2.9
			5	2.57	3	1.2
			6	0.95	0	
			7	2.83	2	7.1
			8	2.03	2	9.9
			Avg	2.69	2.0	5.8
Sodium saccharin	0.2 g		1	2.67	1	3.8
			2	0.83	1	12.0
			3	1.15	1	8.7
			4	1.28	2	15.6
			5	2.00	2	1.0
			6	3.33	3	9.0
			7	2.47	1	4.0
			8	0.76	1	13.2
			9	4.25	5	11.8
			Avg	2.15	1.9	8.8
	1.0 g		1	0.27	0	
			2	2.11	2	9.5
			3	1.67	1	6.0
			4	1.67	2	12.0
			5	1.50	1	6.7
			6	3.12	3	9.6
			7	2.43	2	8.2
			Avg	1.82	1.6	7.4
	5.0 g		1	3.56	2	5.6
			2	4.82	5	10.4
			3	1.43	1	7.0
			4	3.13	3	9.6
			5	0.72	1	13.9
			6	4.47	4	8.9
			7	2.26	3	13.3
			8	1.03	0	
			Avg	2.68	2.4	8.6

Table 7
 IN VITRO ASSAYS OF SODIUM SACCHARIN WITH
5 STRAINS OF SALMONELLA TYPHIMURIUM

Experiment Number	Compound	Amount added/plate	Metabolic Activation	<u>His⁺</u> Revertants per Plate				
				TA1530	TA1535	TA1536	TA1537	TA1538
1	Negative Control	5 μ g	-	53	19	2	22	16
			+	60	31	3	7	11
2	Sodium saccharin	100 mg	-	48	16	0	4	14
			+	40	9	0	3	11
2	Negative Control	N-Methyl-N'-nitro-N-nitrosoguanidine (crystal added to center of plate)	-	10	-	-	4	-
			+	22	-	-	7	-
2	Ethyl methane sulfonate (10 μ l added to 6 mm sterile filter disc)	-	-	-	*	-	-	*
			+	-	*	-	-	-
2	Dimethylnitrosamine (10 μ l added to 6 mm sterile filter disc)	-	-	-	-	-	-	-
			+	-	*	-	-	-
2	Sodium saccharin	100 mg	-	-	2	-	4	-
			+	-	1	-	1	-

* + indicates a ring of mutants around the spot where the chemical was added.

- indicates no ring of mutants.

Table 8
IN VITRO ASSAY OF SODIUM SACCHARIN WITH
SACCHAROMYCES CEREV рИIAE D3

Compound	Percent Concentration (w/v or v/v)	CFU (x 10 ⁷)	Ade	Percent Survivors	Ade
			Recombinants (x 10 ³)		Recombinants per 10 ⁵ CFU
Negative Control		8.17	4.5	100%	5.1
EMS (Positive Control)	1%	4.80	119	59	248
Sodium saccharin	5	5.50	6	67	10.9

A minimum of 110,000 colonies were scanned for mitotic recombinants.

DOMINANT LETHAL STUDY - RAT

TABLE 9
AVERAGE IMPLANTATIONS PER PREGNANT FEMALE

WEEK	CONTROL	71-11		200 MG/KG		71-11		1 G/KG		COMPOUND FDA NO	SODIUM SACCHARIN 71-11	TEM	.2 MG/KG
		71-11	200 MG/KG	71-11	200 MG/KG	71-11	200 MG/KG	71-11	5 G/KG				
SINGLE TREATMENT													
1	177/ 15=11.84	186/ 16=11.62		215/ 18=11.94		249/ 20=12.45		201/ 17=11.82					
2	214/ 20=10.70	230/ 19=12.11		226/ 19=11.89		234/ 20=11.70		202/ 20=10.10					
3	245/ 20=12.25	238/ 20=11.90		247/ 20=12.35		245/ 20=12.25		147/ 20= 7.35 **					
4	237/ 20=11.85	236/ 20=11.80		217/ 19=11.42		255/ 20=12.75		103/ 17= 6.66 **					
5	246/ 20=12.30	256/ 20=12.80		257/ 20=12.85		280/ 20=14.00 *I		226/ 20=11.30					
6	230/ 20=11.50	244/ 20=12.20		203/ 17=11.94		203/ 18=11.28		253/ 20=12.65 *I					
7	226/ 20=11.30	248/ 20=12.40		227/ 20=11.35		240/ 19=12.63		261/ 20=13.05					
8	249/ 20=12.45	242/ 20=12.10		256/ 20=12.80		264/ 20=13.20		247/ 20=12.35					
MULTIPLE TREATMENT													
1	223/ 20=11.16	219/ 19=11.53		171/ 14=12.21		182/ 16=11.37							
2	249/ 20=12.45	235/ 20=11.75		251/ 20=12.55		209/ 20=10.45 *							
3	235/ 20=11.75	232/ 20=11.60		242/ 20=12.10		245/ 20=12.25							
4	248/ 20=12.40	262/ 20=13.10		262/ 20=13.10		243/ 18=13.50							
5	214/ 16=11.89	235/ 18=13.06		195/ 16=12.19		238/ 20=11.90							
6	244/ 20=12.20	230/ 20=11.50		247/ 20=12.35		247/ 19=13.00							
7	237/ 20=11.85	243/ 20=12.15		234/ 20=11.70		250/ 20=12.50							

* SIGNIFICANT AT P LT 0.05

** SIGNIFICANT AT P LT 0.01

I INCREASED ABOVE CONTROL

DOMINANT LETHAL STUDY - RAT

TABLE 10
AVERAGE DEAD IMPLANTS PER PREGNANT FEMALE

WEEK	CONTROL	71-11		1 G/KG	71-11	5 G/KG	TEM	.2 MG/KG	SODIUM SACCHARIN - 71-11
		COMPOUND FDA NO							
SINGLE TREATMENT									
1	6/ 15± .48	10/ 16± .63		5/ 10± .28		14/ 20± .70		55/ 17± 3.24 **	
2	8/ 20± .48	16/ 19± .84		14/ 19± .74		15/ 20± .75		133/ 20± 6.65 **	
3	16/ 26± .80	12/ 20± .60		12/ 20± .60		9/ 20± .45		119/ 20± 5.95 **	
4	9/ 20± .45	23/ 20± 1.15		15/ 19± .79		26/ 20± 1.30		92/ 17± 5.41 **	
5	24/ 20± 1.20	18/ 20± .90		11/ 20± .55		12/ 20± .60		60/ 20± 3.00 **	
6	15/ 20± .75	18/ 20± .90		15/ 17± .88		24/ 18± 1.33		7/ 20± .35	
7	7/ 20± .35	7/ 20± .35		7/ 20± .35		7/ 19± .37		14/ 20± .70	
8	23/ 20± 1.15	17/ 20± .85		15/ 20± .75		20/ 20± 1.00		18/ 20± .90	
MULTIPLE TREATMENT									
1	35/ 20± 1.75	14/ 19± .74 D		18/ 14± 1.29		10/ 16± .63 D			
2	22/ 20± 1.10	19/ 20± .95		8/ 20± .40 D		21/ 20± 1.05			
3	18/ 20± .90	9/ 20± .45		11/ 20± .55		21/ 20± 1.05			
4	29/ 20± 1.45	8/ 20± .40 D		16/ 20± .80		16/ 18± .89			
5	15/ 18± .83	14/ 18± .78		12/ 16± .75		16/ 20± .80			
6	10/ 20± .50	14/ 20± .70		20/ 20± 1.00		22/ 19± 1.16			
7	21/ 20± 1.05	15/ 20± .75		11/ 20± .55		16/ 20± .80			

* SIGNIFICANT AT P LT 0.05

** SIGNIFICANT AT P LT 0.01

D DECREASED BELOW CONTROL

DOMINANT LETHAL STUDY - RAT

TABLE II

DEAD IMPLANTS/TOTAL IMPLANTS

WEEK	CONTROL	71-11		200 MG/KG		71-11		1 G/KG		71-11		5 G/KG		TEM		.2 MG/KG		
		71-11	200 MG/KG	71-11	200 MG/KG	71-11	200 MG/KG	71-11	200 MG/KG	71-11	200 MG/KG	SODIUM SACCHARIN 71-11	FDA NO	71-11	200 MG/KG	71-11	200 MG/KG	
SINGLE TREATMENT																		
6	1	6/ 177=	.03	10/ 186=	.05			5/ 215=	.02			14/ 249=	.06			55/ 201=	.27	**
	2	8/ 214=	.04	16/ 230=	.07			14/ 226=	.06			15/ 234=	.06			133/ 202=	.66	**
	3	16/ 245=	.07	12/ 238=	.05			12/ 247=	.05			9/ 245=	.04			119/ 147=	.41	**
	4	9/ 237=	.04	23/ 236=	.10			15/ 217=	.07			26/ 255=	.10			92/ 103=	.89	**
	5	24/ 246=	.10	18/ 256=	.07			11/ 257=	.04			12/ 280=	.04			60/ 226=	.27	**
	6	15/ 230=	.07	18/ 244=	.07			15/ 203=	.07			24/ 203=	.12			7/ 253=	.03	*D
	7	7/ 226=	.03	7/ 248=	.03			7/ 227=	.03			7/ 240=	.03			14/ 261=	.05	
	8	23/ 249=	.09	17/ 242=	.07			15/ 256=	.06			20/ 264=	.08			16/ 247=	.07	
MULTIPLE TREATMENT																		
6	1	35/ 223=	.16	14/ 219=	.06			18/ 171=	.11			10/ 182=	.05	*D				
	2	22/ 249=	.09	19/ 235=	.08			8/ 251=	.03	*D		21/ 209=	.10					
	3	18/ 235=	.08	9/ 232=	.04			11/ 242=	.05			21/ 245=	.09					
	4	29/ 248=	.12	8/ 262=	.03	*D		16/ 262=	.06			16/ 243=	.07					
	5	15/ 214=	.07	14/ 235=	.06			12/ 195=	.06			16/ 238=	.07					
	6	10/ 244=	.04	14/ 230=	.06			20/ 247=	.08			22/ 247=	.09					
	7	21/ 237=	.09	15/ 243=	.06			11/ 234=	.05			16/ 250=	.06					

* SIGNIFICANT AT P LT 0.05

** SIGNIFICANT AT P LT 0.01

D DECREASED BELOW CONTROL

DOMINANT LETHAL STUDY - RAT

TABLE 12

AVERAGE CORPORA LUTEA PER PREGNANT FEMALE

WEEK	CONTROL	71-11	200 MG/KG	71-11	1 G/KG	71-11	5 G/KG	TEM	.2 MG/KG	COMPOUND FDA NO	SODIUM SACCHARIN 71-11
SINGLE TREATMENT											
1	194/ 15=12.93	206/ 16=12.87		228/ 18=12.67		263/ 20=13.15		226/ 17=13.29			
2	245/ 20=12.25	259/ 19=13.63 *		260/ 19=13.68 *		269/ 20=13.45 *		255/ 20=12.75			
3	256/ 20=12.80	263/ 20=13.15		265/ 20=13.25		257/ 20=12.85		221/ 20=11.05 **			
4	250/ 20=12.50	256/ 20=12.80		235/ 19=12.37		268/ 20=13.40		205/ 17=12.06			
5	274/ 20=13.70	271/ 20=13.55		268/ 20=13.40		300/ 20=15.00 *		250/ 20=12.50 *			
6	250/ 20=12.50	279/ 20=13.95 **		210/ 17=12.35		235/ 18=13.06		265/ 20=13.25			
7	262/ 20=13.10	270/ 20=13.50		259/ 20=12.95		246/ 19=12.95		274/ 20=13.70			
8	258/ 20=12.90	263/ 20=13.15		285/ 20=14.25 *		285/ 20=14.25 **		269/ 20=13.45			
MULTIPLE TREATMENT											
1	254/ 20=12.70	241/ 19=12.68		184/ 14=13.14		197/ 16=12.31					
2	265/ 20=13.25	255/ 20=12.75		275/ 20=13.75		264/ 20=13.20					
3	256/ 20=12.80	269/ 20=13.45		264/ 20=13.20		257/ 20=12.85					
4	296/ 20=14.00	291/ 20=14.55		284/ 20=14.20		257/ 18=14.28					
5	258/ 18=14.33	265/ 18=14.72		230/ 16=14.38		265/ 20=13.25					
6	266/ 20=13.30	255/ 20=12.75		264/ 20=13.20		258/ 19=13.58					
7	260/ 20=13.00	267/ 20=13.35		277/ 20=13.05		267/ 20=13.35					

* SIGNIFICANT AT P LT 0.05

** SIGNIFICANT AT P LT 0.01

DOMINANT LETHAL STUDY - RAT

TABLE 13

AVERAGE PREIMPLANTATION LOSS PER PREGNANT FEMALE

WEEK	CONTROL	71-11		200 MG/KG		71-11		1 G/KG		71-11		5 G/KG		TEM		.2 MG/KG		
		71-11	200 MG/KG	71-11	200 MG/KG	71-11	200 MG/KG	71-11	200 MG/KG	71-11	200 MG/KG	71-11	200 MG/KG	71-11	200 MG/KG	71-11	200 MG/KG	
SINGLE TREATMENT																		
1	17/ 20= 1.13		20/ 16= 1.25		13/ 18= .72		14/ 20= .70		25/ 17= 1.47		53/ 20= 2.65*		53/ 20= 2.65*		53/ 20= 2.65*		53/ 20= 2.65*	
2	31/ 20= 1.55		29/ 19= 1.53		34/ 19= 1.79		35/ 20= 1.75		74/ 20= 3.70**		102/ 17= 6.00**		102/ 17= 6.00**		102/ 17= 6.00**		102/ 17= 6.00**	
3	11/ 20= .55		25/ 20= 1.25		18/ 20= .90		12/ 20= .60		74/ 20= 3.70**		13/ 20= .65		13/ 20= .65		13/ 20= .65		13/ 20= .65	
4	13/ 20= .65		20/ 20= 1.00		10/ 19= .95		13/ 20= .65		24/ 20= 1.20		12/ 20= .60		12/ 20= .60		12/ 20= .60		12/ 20= .60	
5	28/ 20= 1.40		15/ 20= .75		11/ 20= .55		20/ 20= 1.00		24/ 20= 1.20		32/ 18= 1.78		13/ 20= .65		13/ 20= .65		13/ 20= .65	
6	20/ 20= 1.00		35/ 20= 1.75		7/ 17= .41		32/ 18= 1.78		12/ 20= .60		6/ 19= .32 D		22/ 20= 1.10		22/ 20= 1.10		22/ 20= 1.10	
7	36/ 20= 1.80		22/ 20= 1.10		32/ 20= 1.60		6/ 19= .32 D		13/ 20= .65		21/ 20= 1.05		21/ 20= 1.05		21/ 20= 1.05		21/ 20= 1.05	
8	9/ 20= .45		21/ 20= 1.05		29/ 20= 1.45		21/ 20= 1.05		22/ 20= 1.10		12/ 20= .60		12/ 20= .60		12/ 20= .60		12/ 20= .60	
MULTIPLE TREATMENT																		
1	31/ 20= 1.55		22/ 19= 1.16		13/ 14= .93		15/ 16= .94		55/ 20= 2.75		12/ 20= .60		12/ 20= .60		12/ 20= .60		12/ 20= .60	
2	16/ 20= .80		20/ 20= 1.00		24/ 20= 1.20		55/ 20= 2.75		27/ 20= 1.35		11/ 19= .58		11/ 19= .58		11/ 19= .58		11/ 19= .58	
3	21/ 20= 1.05		37/ 20= 1.85		22/ 20= 1.10		12/ 20= .60		14/ 18= .78		17/ 20= 1.20		17/ 20= 1.20		17/ 20= 1.20		17/ 20= 1.20	
4	48/ 20= 2.40		29/ 20= 1.45		22/ 20= 1.10		14/ 18= .78		17/ 20= 1.20		17/ 20= 1.20		17/ 20= 1.20		17/ 20= 1.20		17/ 20= 1.20	
5	44/ 18= 2.44		30/ 18= 1.67		35/ 16= 2.19		27/ 20= 1.35		17/ 20= 1.20		17/ 20= 1.20		17/ 20= 1.20		17/ 20= 1.20		17/ 20= 1.20	
6	22/ 20= 1.10		25/ 20= 1.25		17/ 20= .85		11/ 19= .58		17/ 20= 1.20		17/ 20= 1.20		17/ 20= 1.20		17/ 20= 1.20		17/ 20= 1.20	
7	23/ 20= 1.15		24/ 20= 1.20		43/ 20= 2.15		17/ 20= .85		17/ 20= 1.20		17/ 20= 1.20		17/ 20= 1.20		17/ 20= 1.20		17/ 20= 1.20	

* SIGNIFICANT AT P LT 0.05

** SIGNIFICANT AT P LT 0.01

D DECREASED BELOW CONTROL

DOMINANT LETHAL STUDY OF COMPOUND 71-11 SODIUM SACCHARIN
TABLE 14

CHI-SQUARE TEST OF THE FERTILITY INDEX (1 DEGREE OF FREEDOM)

WEEK	VEHICLE CONTROL				71-11 200 MG/KG				71-11 1 G/KG				71-11 5 G/KG				TEM .2 MG/KG				
	N	N	FERT.		N	N	FERT.		N	N	FERT.		N	N	FERT.		N	N	FERT.		
	PRG	MTD	INDEX	CHISQ	PRG	MTD	INDEX	CHISQ	PRG	MTD	INDEX	CHISQ	PRG	MTD	INDEX	CHISQ	PRG	MTD	INDEX	CHISQ	
SINGLE TREATMENT																					
42	1	15	20	.75	0.00	16	20	.80	0.00	18	20	.90	.69	20	20	1.00	3.66	17	20	.85	.16
	2	20	20	1.00	0.00	19	20	.95	0.00	19	20	.95	0.00	20	20	1.00	0.00	20	20	1.00	0.00
	3	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00
	4	20	20	1.00	0.00	20	20	1.00	0.00	19	20	.95	0.00	20	20	1.00	0.00	17	20	.85	1.44
	5	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00
	6	20	20	1.00	0.00	20	20	1.00	0.00	17	20	.85	1.44	18	20	.90	.53	20	20	1.00	0.00
	7	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	19	20	.95	0.00	20	20	1.00	0.00
	8	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00
MULTIPLE TREATMENT																					
	1	20	20	1.00	0.00	19	20	.95	0.00	14	20	.70	4.90*	16	20	.80	2.50				
	2	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00				
	3	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00				
	4	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	18	20	.90	.53				
	5	18	20	.90	0.00	18	20	.90	.28	16	20	.80	.20	20	20	1.00	.53				
	6	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	19	20	.95	0.00				
	7	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00				

* SIGNIFICANT AT P LT 0.05

DOMINANT LETHAL STUDY OF COMPOUND 71-11 SODIUM SACCHARIN

TABLE 15
CHI-SQUARE TEST OF THE DEATH INDEX (1 DEGREE OF FREEDOM)

WEEK	VEHICLE CONTROL				71-11 200 MG/KG				71-11 1 G/KG				71-11 5 G/KG				TEM .2 MG/KG			
	N WDI	N PRG	DEATH INDEX	CHISQ	N WDI	N PRG	DEATH INDEX	CHISQ	N WDI	N PRG	DEATH INDEX	CHISQ	N WDI	N PRG	DEATH INDEX	CHISQ	N WDI	N PRG	DEATH INDEX	CHISQ
SINGLE TREATMENT																				
1	4	15	.27	0.00	6	16	.38	.07	4	18	.22	.01	8	20	.40	.21	13	17	.76	6.06 *
2	5	20	.25	0.00	10	19	.53	2.08	8	19	.42	.63	8	20	.40	.46	16	20	.80	10.03 **
3	7	20	.35	0.00	11	20	.55	.91	10	20	.50	.41	7	20	.35	.11	18	20	.90	10.67 **
4	8	20	.40	0.00	11	20	.55	.40	8	19	.42	.04	13	20	.65	1.60	17	17	1.00	12.48 **
5	11	20	.55	0.00	7	20	.35	.91	8	20	.40	.40	8	20	.40	.40	16	20	.80	1.82
6	11	20	.55	0.00	13	20	.65	.10	7	17	.41	.26	11	18	.61	.00	5	20	.25	2.60
7	7	20	.35	0.00	7	20	.35	.11	6	20	.30	0.00	6	19	.32	.01	10	20	.50	.41
8	10	20	.50	0.00	9	20	.45	0.00	8	20	.40	.10	9	20	.45	0.00	10	20	.50	.10
MULTIPLE TREATMENT																				
1	15	20	.75	0.00	11	19	.58	.63	6	14	.63	2.37	7	16	.44	2.40				
2	13	20	.65	0.00	10	20	.50	.41	7	20	.35	2.50	10	20	.50	.41				
3	8	20	.40	0.00	7	20	.35	0.00	7	20	.35	0.00	12	20	.60	.90				
4	12	20	.60	0.00	6	20	.30	2.53	11	20	.55	0.00	9	18	.50	.09				
5	8	18	.44	0.00	7	18	.39	0.00	8	16	.50	0.00	8	20	.40	.00				
6	6	20	.30	0.00	9	20	.45	.43	7	20	.35	0.00	11	19	.58	2.05				
7	9	20	.45	0.00	7	20	.35	.10	9	20	.45	.10	8	20	.40	0.00				

* SIGNIFICANT AT P LT 0.05

** SIGNIFICANT AT P LT 0.01

Table 16
SODIUM SACCHARIN TRANSLOCATION STUDY--SUMMARY OF BREEDING AND LITTER DATA
 F_0 GENERATION MICE

<u>Parameter</u>	<u>Control I</u>	<u>Control II</u>	<u>TEM^a I (0.32 mg/1--4 wks)</u>	<u>TEM^a II (0.32 mg/1--2 wks) (0.12 mg/1--2 wks)</u>	<u>71-11^b (1000 ppm)</u>	<u>71-11^b (5000 ppm)</u>
Number of F_0 males	40	40	40	60	79	79
Number of F_0 females	81	80	81	180	158	158
Number pregnant	71	69	11	150	134	139
Percent pregnant	88	86	14	83	85	87
Number of nonbreeder males	1	2	31	3	4	3
Percent nonbreeders	2.5	5.0	77.5	5.0	5.1	3.8
Average litter size	10.0	10.20	2.36	7.24	9.85	9.75
Average number males/litter	5.15	5.39	0.73	3.71	4.67	4.33
Average number females/litter	4.77	4.81	1.45	3.53	4.47	4.76

^aTriethylenemelamine (TEM)

^bSodium Saccharin (71-11)

Table 17
SODIUM SACCHARIN TRANSLOCATION STUDY--MOUSE LITTER SIZE DISTRIBUTION OF YOUNG DERIVED FROM F₀ GENERATION ADULTS

Litter Size	Control I	Control II	TEM ^a I (0.32 mg/l--4 wks)	TEM ^a II (0.32 mg/l--2 wks) (0.12 mg/l--2 wks)	71-11 ^b (1000 ppm)	71-11 ^b (5000 ppm)
1	0	0	2	2	0	0
2	0	0	1	3	0	1
3	0	0	0	3	2	3
4	0	3	1	9	0	0
5	1	2	1	10	1	1
6	4	0	1	16	3	3
7	5	0	1	29	3	5
8	6	3	0	19	11	8
9	8	8	0	23	24	23
10	15	21	0	16	31	32
11	13	15	0	6	36	25
12	9	12	0	6	15	24
13	3	3	0	1	4	8
14	4	2	0	1	2	2
15	2	0	0	0	0	0
16	0	0	0	0	0	0
17	0	0	0	0	0	0
18	0	0	0	0	0	0
Mean (μ)	10.14	10.20	3.71	7.54	10.00	10.03
Variance (σ^2)	5.14	4.37	5.83	6.13	3.28	4.51
Standard deviation (σ)	2.27	2.09	2.41	2.48	1.81	2.12

^aTriethylenemelamine (TEM)

^bSodium Saccharin (71-11)

Table 18
SODIUM SACCHARIN TRANSLOCATION STUDY--MOUSE SUMMARY BREEDING DATA OF F₁ GENERATION

<u>Parameter</u>	<u>Control I</u>	<u>Control II</u>	<u>TEM^a I (0.32 mg/1--4 wks)</u>	<u>TEM^a II (0.32 mg/1--2 wks) (0.12 mg/1--2 wks)</u>	<u>71-11^b (1000 ppm)</u>	<u>71-11^b (5000 ppm)</u>
Number of F ₁ males	97	100	8	112	200	200
Number of F ₁ females	297	300	24	336	600	600
Number of mating plugs	244	267	16	281	546	523
Percent mating plugs	82	89	67	84	91	87
Number of pregnant females	256	242	13	268	526	528
Percent pregnant	86	81	54	80	88	88
Number pregnant with mating plugs	240	240	12	257	512	503
Percent pregnant with mating plugs	94	99	92	96	85	84
Number pregnant without mating plugs	16	2	1	11	15	25
Percent pregnant without mating plugs	6	1	8	4	2	4
Number of females not pregnant	41	58	11	68	73	72
Percent females not pregnant	14	19	46	20	12	12
Number not pregnant with mating plugs	4	27	4	24	33	20
Percent not pregnant with mating plugs	10	46	36	35	6	3
Nonbreeder and sterile males	5	0	2	3	1	7
Percent nonbreeder and sterile males	5	0	25	3	0.5	1

^aTriethylenemalamine (TEM)

^bSodium saccharin (71-11)

Table 19
SODIUM SACCHARIN TRANSLOCATION STUDY--MOUSE LITTER SIZE DISTRIBUTION OF YOUNG DERIVED FROM F₁ GENERATION ADULTS

<u>Litter Size</u>	<u>Control I</u>	<u>Control II</u>	<u>TEM^{a,b} I (0.32 mg/l--4 wks)</u>	<u>TEM^a II (0.32 mg/l--2 wks) (0.12 mg/l--2 wks)</u>	<u>71-11^c (1000 ppm)</u>	<u>71-11^c (5000 ppm)</u>
1	0	1	4	4	2	4
2	1	2	3	6	1	3
3	1	1	2	6	3	7
4	3	3	8	6	5	7
5	2	4	4	10	6	9
6	1	2	4	5	9	2
7	6	7	1	5	19	8
8	7	16	1	14	29	26
9	24	31	1	36	67	54
10	35	49	2	70	110	105
11	49	45	4	41	102	122
12	62	48	4	36	84	97
13	41	21	0	19	48	47
14	14	6	0	5	29	26
15	8	3	0	1	6	5
16	2	1	0	1	2	3
17	0	1	0	0	1	1
18	0	1	0	0	0	0
Mean (μ)	11.18	10.42	6.0	9.58	10.49	10.53
Variance (σ^2)	4.71	5.64	13.30	8.10	5.14	5.87
Standard deviation (σ)	2.17	2.37	3.65	2.85	2.27	2.42

^aTriethylenemalamine (TEM)

^bTotal of three matings--9 females per male--8 males.

^cSodium saccharin (71-11)

Table 20
SODIUM SACCHARIN TRANSLOCATION STUDY--SUMMARY OF DEAD IMPLANT OCCURRENCE PER F₁ MALE MOUSE

<u>Parameter</u>	<u>Control I</u>	<u>Control II</u>	<u>TEM^a I (0.32 mg/1--4 wks)</u>	<u>TEM^a II (0.32 mg/1--2 wks) (0.12 mg/1--2 wks)</u>	<u>71-11^b (1000 ppm)</u>	<u>71-11^b (5000 ppm)</u>
Number of F ₁ males	99	100	8	112	200	200
♂'s having ♀s with no dead implants	35	40	1	36	69	69
♂'s having ♀s with 1 dead implant	29	32	1	41	72	55
♂'s having ♀s with 2 dead implants	18	17	0	10	36	43
♂'s having ♀s with 3 dead implants	7	5	0	6	12	15
♂'s having ♀s with 4 dead implants	2	6	0	4	7	2
♂'s having ♀s with 5 dead implants	2	0	0	0	0	4
♂'s having ♀s with more than 5 dead implants	1	0	4	12	3	4

^aTriethylenemelamine (TEM)

^bSodium saccharin (71-11)

Table 21
SODIUM SACCHARIN TRANSLOCATION STUDY--SUMMARY OF DEAD IMPLANTS PER PREGNANT FEMALE
(FIRST BREEDING OF FEMALES TO F₁ MALES)

<u>Parameter</u>	<u>Control I</u>	<u>Control II</u>	<u>TEM^a I</u> (0.32 mg/1--4 wks)	<u>TEM^a II</u> (0.32 mg/1--2 wks) (0.12 mg/1--2 wks)	<u>71-11^b</u> (1000 ppm)	<u>71-11^b</u> (5000 ppm)
Number of pregnant females	256	242	13	268	526	528
♀s with no dead implants	175	160	3	160	350	361
♀s with 1 dead implant	61	62	1	64	140	121
♀s with 2 dead implants	14	17	0	14	26	34
♀s with 3 dead implants	4	3	0	7	4	5
♀s with 4 dead implants	1	0	3	5	1	2
♀s with 5 dead implants	1	0	0	1	1	1
♀s with more than 5 dead implants	0	0	6	17	4	4

Table 22
SODIUM SACCHARIN TRANSLOCATION STUDY--SUMMARY OF PRESUMPTIVE TRANSLOCATION F₁ MALES AFTER TWO BREEDINGS

<u>Parameter</u>	<u>Control I</u>	<u>Control II</u>	<u>TEM^a I</u> (0.32 mg/1--4 wks)	<u>TEM^a II</u> (0.32 mg/1--2 wks) (0.12 mg/1--2 wks)	<u>71-11^b</u> (1000 ppm)	<u>71-11^b</u> (5000 ppm)
Total number of F ₁ males	99	100	8	112	200	200
Number of nonbreeder males	2	0	1	0	0	1
Number of presumptive sterile males	0	0	0	3	0	0
Number of partially sterile males	0	1	5	11	3	1

^aTriethylenemelamine (TEM)

^bSodium Saccharin (71-11)

Table 23

SODIUM SACCHARIN TRANSLOCATION STUDY--INDIVIDUAL IDENTIFICATION OF NONBREEDER, PRESUMPTIVE STERILE,
AND PARTIALLY STERILE F₁ MALES AFTER TWO BREEDINGS

<u>Control I</u>	<u>Control II</u>	<u>TEM^a I (0.32 mg/l--4 wks)</u>	<u>TEM^a II (0.32 mg/l--2 wks) (0.12 mg/l--2 wks)</u>	<u>71-11^b (1000 ppm)</u>	<u>71-11^b (5000 ppm)</u>
<u>NON-BREEDER</u>					
15		102			1033
40					
<u>PRESUMPTIVE STERILE</u>					
1455					
101			1504		
103			1546		
106			1590		
107					
108					
<u>PARTIALLY STERILE</u>					
101		1515		1307	1169
103		1528		1343	
106		1544		1389	
107		1561			
108		1565			
		1571			
		1572			
		1595			
		1602			
		1605			
		1612			

^aTriethylenemelamine (TEM)

^bSodium Saccharin (71-11)

Table 24

SODIUM SACCHARIN TRANSLOCATION STUDY--BREEDING AND REBREEDING SUMMARY
OF NONBREEDER AND PRESUMPTIVE TRANSLOCATION F₁ MALES--CONTROLS

Treatment Group	F ₁ Male Number	First Breeding (3 females)			Second Breeding (3 females)		
Control I	15	-*	-	-	-	-	-
	16	-	-	-	10	-	-
	40	-	-	-	-	-	-
	41	-	-	-	10	-	-
	69	-	-	-	11	12	11
	77	<u>6</u>	<u>4</u>	<u>8</u>	<u>7</u>	<u>11</u>	-
Totals		6			2		
Control II	1403	0**	9	0	9	-	-
	1423	0	0	9	10	11	11
	1455	0	7	7	-	-	-
	1484	0	9	9	-	-	8
	1491	0	9	-	10	12	10
	1495	<u>2</u>	<u>5</u>	<u>0</u>	<u>12</u>	<u>10</u>	<u>2</u>
Totals		6			1		

* - indicates a plug was not detected and female was not pregnant.

**0 indicates a plug was observed but female was not pregnant.

Table 25

SODIUM SACCHARIN TRANSLOCATION STUDY--BREEDING AND REBREEDING SUMMARY OF
NONBREEDER AND PRESUMPTIVE TRANSLOCATION F₁ MALES--POSITIVE CONTROLS

Treatment Group	F ₁ Male Number	First Breeding (3 females)	Second Breeding (3 females)	Third Breeding (3 females)
TEM I (0.32 mg/l for 4 weeks)	101	0 ** 0 0	0 4 - *	4 1 6
	102	- - -	- - -	- - -
	103	- 1 -	5 5 0	4 4 2
	106	4 5 3	0 4 7	6 5 6
	107	0 - -	1 - -	- - -
	108	<u>2 8 6</u>	<u>4 4 1</u>	<u>0 2 -</u>
Totals		6	6	6
TEM II (0.32 mg/l for 2 weeks, 0.12 mg/l for 2 weeks)	1504	0 0 -	0 0 0	
	1515	3 3 4	5 4 2	
	1528	0 2 0	0 1 -	
	1544	4 2 1	3 0 5	
	1546	0 0 0	0 0 -	
	1551	0 - -	0 12 10	
	1561	4 3 -	4 3 3	
	1565	0 4 2	4 2 1	
	1571	1 6 8	3 3 4	
	1572	5 2 6	- - -	
	1576	9 5 6	8 8 -	
	1590	0 0 0	0 0 0	
	1595	5 2 3	2 3 -	
	1599	9 4 -	12 12 -	
	1602	3 0 6	2 0 7	
	1605	5 0 2	- - -	
	1612	<u>5 3 -</u>	<u>0 3 4</u>	
Totals		17	14	

* - indicates a plug was not detected and female was not pregnant.

**0 indicates a plug was observed but female was not pregnant.

Table 26

SODIUM SACCHARIN TRANSLOCATION STUDY--BREEDING AND REBREEDING SUMMARY OF
NONBREEDER AND PRESUMPTIVE TRANSLOCATION F₁ MALES--SODIUM SACCHARIN

<u>Treatment Group</u>	<u>F₁ Male Number</u>	<u>First Breeding (3 Females)</u>			<u>Second Breeding (3 Females)</u>		
Sodium Saccharin (1000 ppm)	1254	9	0**	8	8	0	10
	1258	0	8	-*	9	7	7
	1285	6	9	9	10	9	0
	1288	9	7	0	12	12	12
	1289	-	-	-	10	12	9
	1301	8	0	5	12	11	13
	1305	0	9	-	11	10	3
	1307	8	4	9	9	0	-
	1343	0	0	9	0	3	-
	1389	4	6	6	0	0	6
Totals		10			3		
Sodium Saccharin (5000 ppm)	1033	-	-	-	-	-	-
	1043	0	-	-	12	10	10
	1054	-	-	-	8	-	10
	1056	-	-	-	12	11	10
	1084	2	0	-	9	10	9
	1101	0	0	7	8	10	11
	1110	5	5	9	11	9	8
	1169	-	-	-	9	0	9
	1173	9	7	4	12	13	7
	1175	-	-	-	-	-	11
	1179	0	9	9	0	12	5
	1188	-	-	-	7	10	9
Totals		12			2		

* - indicates a plug was not detected and female was not pregnant.

** 0 indicates a plug was observed but female was not pregnant.

Table 27

SODIUM SACCHARIN TRANSLOCATION STUDY--CYTOGENETIC EVALUATION
OF MEIOTIC CELLS FROM TESTES PREPARATIONS OF F₁ MICE

<u>Treatment</u>	<u>F₁ Male Number</u>	<u>Testes Weight (mg)</u>	<u>Classification After Two Breedings</u>	<u>Cytogenetic Classification</u>
Control I	15	272	Nonbreeder	Normal
	40	272	Nonbreeder	Normal
Control II	1455	301	Partially sterile	Normal
TEM I	103	375	Partially sterile	Positive reciprocal translocation
	106	259	Partially sterile	Positive reciprocal translocation
	108	252	Partially sterile	Positive reciprocal translocation
Sodium Saccharin (1000 ppm)	1343	312	Partially sterile	Normal
	1389	271	Partially sterile	Positive reciprocal translocation

APPENDIX A

**STATISTICAL PROCEDURE FOR EVALUATION OF
DOMINANT LETHAL DATA WITH A DESCRIPTION
AND EXPLANATION OF THE COMPUTER PRINTOUTS**

Program Abstract

1. Serial Number: KSH009

2. Title: Chemical Mutagenicity Study

3. Deck Name: KLUTE

4. Abstract: This program performs statistical calculations to determine the mutagenicity of certain chemical compounds.

5. Originator: Jim Eusebio
June 1972

6. Revised: Kathleen S. Himmelberger

7. Date: February 8, 1974

8. Memory Requirements: 134236₈

9. Input: Data deck

10. Output: Printed output listing input data and results of several statistical tests (CHI-SQUARE test, ARMITAGE test, T-test, regression fits, PROBIT analysis, analysis of variance).

11. System: CDC 6400 Scope 3.3
FORTRAN IV

Program Description

The program which performs statistical calculations using the autopsy data of female rats is called KLUTE. KLUTE is written in FORTRAN IV for use on the CDC 6400. Because storage requirements of the program exceeded available memory, it was necessary to use overlays (see SCOPE Reference Manual, 6000 Version 3.3, pp 6-14 to 6-18). Therefore, card decks must be loaded in a specific order.

Although KLUTE was designed to allow as much flexibility in experimentation as possible, there are some criteria which must be satisfied:

1. The maximum number of test groups is included in the first week. After the first week, groups may be terminated. (Some studies mate the single-dose groups for eight weeks and multiple-dose groups for only seven.)
2. There are at most five single-dose groups and five multiple-dose groups. The program will handle experiments using only single-dose groups or multiple-dose groups.
3. A control group exists for single-dose and/or multiple-dose groups.
4. All males in the control group are mated in the first week. If a male should die during or after the first week, no data cards appear for him from that time on; however, there must be at least one data card for him in week one. Control group males are numbered consecutively beginning with 1.
5. Number of each variable should not exceed the following:

<u>Variable</u>	<u>Maximum</u>
Males	20/group
Females	100/week
Weeks in study	8
Females mated to each male	80/8 week period

**STATISTICAL PROCEDURE
FOR EVALUATION OF DOMINANT LETHAL DATA**

Introduction

In order to determine the mutagenic potential of selected food additives and chemicals, Stanford Research Institute has conducted several dominant lethal tests in mice and rats. Although individual tests differed slightly in details, basic test procedures were to administer compounds orally at different dose levels and frequency to groups of males. These males, as well as control group males for both the single and multiple-dose groups, were mated with two virgin females.

In studies using mice, females were examined daily for the presence of a mating plug (readily detectable in the mouse). When a plug was found, the female was replaced with a new virgin female. Fourteen days after identifying the mating plug, the females were sacrificed, and total implants, early deaths, and late deaths were counted. This continuous breeding and examination procedure was continued for seven weeks.

In studies using rats, females were removed after seven days of cohabitation with the males and replaced with new virgin females. Fourteen to eighteen days after first day of breeding, females were sacrificed and total implants, early deaths, late deaths, and total corpora lutea were counted. This procedure was repeated for eight weeks in the single dose groups and seven weeks in the multiple dose groups.

Autopsy data for each female was coded on work sheets and then punched on computer cards. These data cards, as well as a few cards describing the particulars of the project (duration, number of test groups, number of mated females, etc.), comprise the input to the KLUTE program.

Input

Input to the KLUTE program is a card deck, which was briefly described in the introduction.

Output

Output from KLUTE includes a printed list of the input data and results of several statistical tests.

KLUTE performs the following operations (where each statistical calculation is done once for each week's data):

1. The data cards are read and stored in central memory while a check is made to verify that the number of corpora lutea is greater than or equal to the number of implants. If any data fail this check, the run is aborted and the data are returned for review. The entire set of input data is printed out.
2. The fertility index (the number of pregnant females divided by the number of mated females) is calculated.
3. The chi-square test is done to compare each dosage level to the control on fertility. Let:

N_i = no. of mated females at dose level i,

n_i = no. of pregnant females at dose level i.

Then the chi-square 2 x 2 tables are of the form:

$$\begin{bmatrix} n_0 & n_1 \\ N_0 - n_0 & N_1 - n_1 \end{bmatrix}$$

and chi-squared (with 1 degree of freedom) is:

$$x_1^2 = \frac{(N_0 + N_1)(|n_0(N_1 - n_1) - n_1(N_0 - n_0)| - (N_0 + N_1)/2)^2}{(n_0 + n_1)(N_0 - n_0 + N_1 - n_1)(N_0)(N_1)} \quad (\text{corrected for continuity})$$

where the subscript 0 represents the control group.*

For each dosage group (including the control group and TEM), the following is printed out: the number of pregnant females (N PRG), the number of mated females (N MTD), the fertility index and x^2 .

4. Armitage's test for a linear trend in proportions is applied to the fertility index. The formula for this calculation is found on pages 246-248 of "Statistical Calculations" by Snedecor and Cochran, 6th Edition, Iowa State University Press, 1967. Using the notation of (3) above, we have a 2 x 3 contingency table of the form:

	<u>dose 1</u>	<u>dose 2</u>	<u>dose 3</u>	<u>row totals</u>
	n_1	n_2	n_3	t
	$N_1 - n_1$	$N_2 - n_2$	$N_3 - n_3$	$T-t$
Column Totals	N_1	N_2	N_3	T

Armitage's "chi-square" is given as $x_{(C-1)}^2 - x_1^2$, where C=3 and

$$x_1^2 = \frac{T(T\sum nx - t\sum Nx)^2}{t(T-t)(T\sum x^2 - (\sum Nx)^2)}, \quad x_{(C-1)}^2 = \frac{T^2(\sum \frac{n}{N} - \frac{t}{T})^2}{t(T-t)}$$

*In all tests, the single-dose treatment groups are compared with the single-dose control group and the multiple-dose treatment groups compared with the multiple-dose control group.

where $\sum_{i=1}^3 n_i x_i$, $\sum_{i=1}^2 \frac{n_i}{N}$ for $\sum_{i=1}^2 \frac{n_i^2}{N_1}$, etc., and the x_i are the dosage levels.

This calculation is then repeated with x replaced by $\log x$. The Armitage test is also applied to the following 2×4 contingency table:

<u>Control</u>	<u>dose 1</u>	<u>dose 2</u>	<u>dose 3</u>
n_0	n_1	n_2	n_3
$N_0 - n_0$	$N_1 - n_1$	$N_2 - n_2$	$N_3 - n_3$

In this case, $C=4$.

The printout for the Armitage tests includes the degrees of freedom, the number pregnant (N PRG) and the number mated (N MTD) for each of the 3 or 4 groups included in the tests, plus X^2 , $X^2_{(C-1)}$ and their difference (labeled ARMTG CHISQ).

5. The t-test is applied to determine significant differences between the average number of implantations per pregnant female at a dose level, and the average for the control. Let

n_i = no. of pregnant females at dose level i .

u_{ij} = total no. of implantations for pregnant female j of dose i .

Then,

$$\bar{u}_i = \frac{1}{n_i} \sum_{j=1}^{n_i} u_{ij}$$

$$s_i^2 = \sum_{j=1}^{n_i} (u_{ij} - \bar{u}_i)^2$$

The T-statistic for dose i has $n_o + n_i - 2$ degrees of freedom, and is equal to:

$$t_i = \frac{\bar{u}_o - \bar{u}_i}{\sqrt{\left[\frac{s_o^2 + s_i^2}{n_o + n_i - 2} \left(\frac{1}{n_o} + \frac{1}{n_i} \right) \right]^{1/2}}}$$

The t-test printout gives, for each group: the number pregnant (N PRG), the mean and standard deviation of the number of implantations. The absolute value of T and the degrees of freedom (DF) are given for each treatment group and for TEM.

6. A regression fit of the average number of implantations, \bar{u}_i , is made for both the arithmetic and logarithmic dose (X_i and $\log X_i$) to see which is better.

These two fits include the data from the three treatment groups only. A third regression using the X_i as independent variables includes data from the three treatment groups and the control group.

The regressions are computed as follows:

Let N = the number of observations, i.e., the total number of pregnant females in the groups used in the regression.

X_i = the value of the independent variable (dose or log dose) for the i -th female.

U_i = the value of the dependent variable (number of implantations) for the i -th female.

Then,

$$\bar{X} = \bar{x} = \frac{1}{N} \sum_{i=1}^N x_i$$

SD X = standard deviation of the x_i

$$= \left[\frac{1}{N-1} SS_x \right]^{1/2},$$

$$\text{where } SS_x = \sum_{i=1}^N (x_i - \bar{x})^2$$

$$\bar{U} = \bar{u} = \frac{1}{N} \sum_{i=1}^N u_i,$$

SD U = standard deviation of the u_i

$$= \left[\frac{1}{N-1} SS_u \right]^{1/2},$$

$$\text{where } SS_u = \sum_{i=1}^N (u_i - \bar{u})^2,$$

$$\text{and } S_{XU} = \sum_{i=1}^N (x_i - \bar{x})(u_i - \bar{u}).$$

From these quantities, we compute:

B = estimate of the slope of the regression line

$$= S_{XU}/SS_x,$$

A = estimate of the intercept of the regression line

$$= \bar{u} - BX,$$

Also,

$$\begin{aligned} \text{VARU.X} &= \text{variance of } U \text{ about the regression line} \\ &= \frac{\text{SS}_U - (S_{XU})^2 / \text{SS}_X}{N-2} \end{aligned}$$

and from this is computed,

$$\text{VARB} = \text{variance of the estimate, B}$$

$$= \frac{\text{VARU.X}}{\text{SS}_X}$$

$$\text{VARA} = \text{variance of the estimate, A}$$

$$= \text{VARU.X} \left[\frac{1}{N} + \frac{\bar{x}^2}{\text{SS}_X} \right]$$

$$\text{VARUBAR} = \text{variance of } U,$$

$$= \frac{\text{VARU.X}}{N}$$

and

$$\text{CV U.X} = \text{coefficient of variation of } U \text{ about } X$$

$$= \frac{(\text{VARU.X})^{1/2}}{\bar{U}}$$

And finally we have:

T_B = the t-statistic for testing the hypothesis that the regression slope is zero

$$= \frac{B}{\sqrt{\text{VARU}}}$$

DF = number of degrees of freedom for T_B

$$= N - 2$$

7. The preimplantation loss, y_{ij} , is calculated for each pregnant female, j , as the number of corpora lutea, v_{ij} , minus the number of implantations, u_{ij} . Then the Freeman-Tukey transformation is applied to y_{ij} as follows:

$$f_{ij} = \sin^{-1} \sqrt{\frac{y_{ij}}{v_{ij}+1}} + \sin^{-1} \sqrt{\frac{y_{ij}+1}{v_{ij}+1}}$$

The t-test is then applied to the f 's. Let

$$\bar{f}_i = \frac{1}{n_i} \sum_{j=1}^{n_i} f_{ij}$$

$$s_i^2 = \sum_{j=1}^{n_i} (f_{ij} - \bar{f}_i)^2,$$

where n_i , and n_o are defined above (step 3).

Then $t_i = \frac{\bar{f}_o - \bar{f}_i}{\sqrt{\left[\frac{s_o^2 + s_i^2}{n_o + n_i - 2} \left(\frac{1}{n_o} + \frac{1}{n_i} \right) \right]^{1/2}}}$

The printout gives, for each group, the number of pregnant females (N PRG), the mean and standard deviation of the f_{ij} 's. For each treatment group and for TEM, the absolute value of t_i (T), and its degrees of freedom (DF) are given.

8. The number of dead implants, z_{ij} , for each female, j , is the sum of the early and late deaths. The t-test is applied to determine significant differences between the average number of dead implants per pregnant female at a dose level and the average for the control by repeating step 5 above with z_{ij} substituted for u_{ij} .

9. The number of pregnant females with one or more dead implants, m_i , is calculated. In the printout, the m_i are referred to as N WDI (i.e., "number with dead implants").

10. The chi-square test and Armitage's test for a linear trend is calculated for the proportion of pregnant females with one or more dead implants,

$$p_i = \frac{m_i}{n_i}$$

by repeating steps 3 and 4, above, with m_i substituted for n_i , and n_i substituted for N_i .

In the printout, the ratio, p_i , is called the "death index", in analogy with the fertility index.

11. The ratios, p_i , computed above, undergo a probit analysis to determine whether the probit of this proportion is linearly related to the log dose. Computer subroutine PROBT, from the IBM System/360 Scientific Subroutine Package Version III, is used to compute A and B and the χ^2 statistic for the regression equation,

$$P_i = A + B * \log x_i$$

where P_i is derived by the program from

$$\int_{-\infty}^{P_i-5} N_x(0,1)dx = p_i$$

($N_x(0,1)$ is the normal curve, with a mean of 0 and a standard deviation of 1).

12. The number of dead implants, z_{ij} , and the number of total implants, u_{ij} , are calculated for each pregnant female, j. The Freeman-Tukey transformation and subsequent t-test is applied to this data by repeating step 7, above, as follows:

$$f_{ij} = \sin^{-1} \sqrt{\frac{z_{ij}}{u_{ij}+1}} + \sin^{-1} \sqrt{\frac{z_{ij+1}}{u_{ij+1}+1}}$$

$$\bar{f}_i = \frac{1}{n_i} \sum_{j=1}^{n_i} f_{ij}$$

$$s_i^2 = \sum_{j=1}^{n_i} (f_{ij} - \bar{f}_i)^2$$

$$t_i = \frac{\bar{f}_o - \bar{f}_i}{\left[\frac{s_o^2 + s_i^2}{n_o + n_i - 2} \left(\frac{1}{n_o} + \frac{1}{n_i} \right) \right]^{1/2}}$$

13. Five one-way analyses of variance are performed on the control groups' data. The five variables analyzed are:

- a. Number of pregnant females,
- b. Number of implantations per pregnant female,
- c. The pre-implantation loss (as defined in Step 7) per pregnant female,
- d. The number of dead implants per pregnant female,
- e. The ratio of dead implants to the total implants per pregnant female.

In view of the fact that none of the variables on which the one-way analysis of variance have been performed is even approximately normal in distribution, the probability levels associated with these analyses of variances are necessarily approximate.

For case a., R_{kj} equals 1 if female j assigned to male k became pregnant; otherwise R_{kj} equals zero. For cases b. through e. the tabulation is limited to data for pregnant females; i.e., R_{kj} equals the value of the specified variable for female j assigned to male k if the female was pregnant; data for non-pregnant females are excluded.

For case a., L_k equals the number of females assigned to male k. For cases b. through e., L_k equals the number of females assigned to male k that became pregnant.

For each of these variables the ANOVA calculations are as follows:

M is the number of males

$$\bar{R}_k = \frac{1}{L_k} \sum_{j=1}^{L_k} R_{kj}$$

$$\bar{R} = \frac{1}{M} \sum_{k=1}^M \bar{R}_k$$

Then, the sum-of-squares-within-males = $SUMSQ_w$

$$= \sum_{k=1}^M \sum_{j=1}^{L_k} (R_{kj} - \bar{R}_k)^2,$$

the degrees-of-freedom-within-males = DF_w

$$= \sum_{k=1}^M (L_k - 1),$$

and the mean-square-within-males = $MEANSQ_w = \frac{SUMSQ_w}{DF_w}$.

Similarly, the sum-of-squares-between-males = $SUMSQ_B = \sum_{k=1}^M L_k (\bar{R}_k - \bar{R})^2$,

the degrees-of-freedom-between-males = $DF_B = M-1$,

and the mean-square-between-males = $MEANSQ_B = \frac{SUMSQ_B}{DF_B}$.

Finally, the F-ratio is $F = \frac{MEANSQ_B}{MEANSQ_w}$.

In the printout, these quantities are labeled without the subscripts, but the "within" and "between" quantities are identified by the page heading.

Also, the total-sum-of-squares = $SUMSQ_w + SUMSQ_B$.

and its degrees-of-freedom

$$= \sum_{k=1}^M L_k - 1,$$

printed.

14. The t-test is applied to determine significant differences between the average number of corpora lutea per pregnant female at a dose level, and the average for the control. Let

n_i = no. of pregnant females at dose level i.

C_{ij} = total no. of corpora lutea for pregnant female j of dose i.

Then,

$$\bar{C}_i = \frac{1}{n_i} \sum_{j=1}^{n_i} C_{ij}$$

$$S_i^2 = \sum_{j=1}^{n_i} (C_{ij} - \bar{C}_i)^2$$

The T-statistic for dose i has $n_o + n_i - 2$ degrees of freedom, and is equal to:

$$t_i = \frac{\bar{C}_o - \bar{C}_i}{\sqrt{\left[\frac{s_o^2 + s_i^2}{n_o + n_i - 2} \left(\frac{1}{n_o} + \frac{1}{n_i} \right) \right]^{1/2}}}$$

The t-test printout gives, for each group: the number pregnant (N PRG), the mean and standard deviation of the number of corpora lutea. The absolute value of T and the degrees of freedom (DF) are given for each treatment group and for TEM.

APPENDIX B
RAW DATA AND STATISTICAL ANALYSES

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	R	L	R
CONTROL	1	S 0.00000	1	1	Y	5	7	0	0	0	0	5
CONTROL	1	S 0.00000	1	2	N	0	0	0	0	0	0	0
CONTROL	1	S 0.00000	2	3	N	0	0	0	0	0	0	0
CONTROL	1	S 0.00000	2	4	Y	6	9	0	0	0	0	6
CONTROL	1	S 0.00000	3	5	Y	6	8	0	0	0	0	6
CONTROL	1	S 0.00000	3	6	Y	5	6	0	0	0	0	5
CONTROL	1	S 0.00000	4	7	Y	0	0	0	0	0	0	0
CONTROL	1	S 0.00000	4	8	Y	9	6	1	0	1	1	9
CONTROL	1	S 0.00000	5	9	Y	4	8	0	0	0	1	5
CONTROL	1	S 0.00000	5	10	N	0	0	0	0	0	0	0
CONTROL	1	S 0.00000	6	11	Y	7	7	0	0	0	0	7
CONTROL	1	S 0.00000	6	12	Y	8	4	0	0	0	0	8
CONTROL	1	S 0.00000	7	13	Y	4	5	0	0	0	0	4
CONTROL	1	S 0.00000	7	14	Y	5	6	0	0	0	0	5
CONTROL	1	S 0.00000	8	15	Y	5	5	0	0	0	0	6
CONTROL	1	S 0.00000	8	16	Y	0	1	0	0	0	0	9
CONTROL	1	S 0.00000	9	17	Y	7	6	0	0	1	0	7
CONTROL	1	S 0.00000	9	18	Y	7	8	0	0	0	0	8
CONTROL	1	S 0.00000	10	19	N	0	0	0	0	0	0	0
CONTROL	1	S 0.00000	10	20	Y	6	7	0	0	1	0	6
71-11	1	S .20000	21	41	Y	6	7	0	0	0	0	6
71-11	1	S .20000	21	42	Y	5	9	0	0	0	0	5
71-11	1	S .20000	22	43	Y	6	4	1	0	0	0	7
71-11	1	S .20000	22	44	Y	7	6	0	0	0	0	8
71-11	1	S .20000	23	45	Y	6	0	0	0	0	1	6
71-11	1	S .20000	23	46	Y	6	6	0	0	0	0	6
71-11	1	S .20000	24	47	Y	6	9	0	0	0	0	8
71-11	1	S .20000	24	48	Y	2	8	0	0	0	0	4
71-11	1	S .20000	25	49	Y	8	4	0	0	0	0	8
71-11	1	S .20000	25	50	N	0	0	0	0	0	0	0
71-11	1	S .20000	26	51	Y	6	7	0	0	0	0	6
71-11	1	S .20000	26	52	Y	5	5	0	0	0	0	6
71-11	1	S .20000	27	53	Y	6	6	0	0	0	0	7
71-11	1	S .20000	27	54	N	0	0	0	0	0	0	0
71-11	1	S .20000	28	55	Y	4	7	0	0	2	3	4
71-11	1	S .20000	28	56	Y	4	8	0	0	0	0	4
71-11	1	S .20000	29	57	Y	5	7	0	0	0	1	5
71-11	1	S .20000	29	58	Y	0	0	0	0	0	0	0
71-11	1	S .20000	30	59	N	0	0	0	0	0	0	0
71-11	1	S .20000	30	60	N	0	0	0	0	0	0	0

DOMINANT LETHAL STUDY OF COMPOUND 71-11

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TFST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		COMPOUNA LUTEA		
							L	R	L	R	L	R	
71-11	1	S 1.00000	31	61	Y	5	5	0	0	2	0	5	5
71-11	1	S 1.00000	31	62	YY	6	7	0	0	0	0	6	7
71-11	1	S 1.00000	32	63	Y	5	7	0	0	0	0	5	7
71-11	1	S 1.00000	32	64	YY	4	4	0	0	0	0	4	7
71-11	1	S 1.00000	33	65	Y	7	4	0	0	0	0	7	5
71-11	1	S 1.00000	33	66	YY	7	4	0	0	0	0	7	4
71-11	1	S 1.00000	34	67	Y	5	9	0	0	0	1	6	10
71-11	1	S 1.00000	34	68	YY	4	8	0	0	0	0	4	8
71-11	1	S 1.00000	35	69	Y	6	5	0	0	0	0	6	6
71-11	1	S 1.00000	35	70	Y	5	8	0	0	0	1	5	9
71-11	1	S 1.00000	36	71	YY	5	7	0	0	0	0	7	8
71-11	1	S 1.00000	36	72	Y	6	8	0	0	0	0	7	8
71-11	1	S 1.00000	37	73	YY	4	9	0	0	0	0	4	9
71-11	1	S 1.00000	37	74	Y	4	8	0	0	0	0	4	8
71-11	1	S 1.00000	38	75	YY	8	5	0	0	0	0	8	5
71-11	1	S 1.00000	38	76	N	0	0	0	0	0	0	0	0
71-11	1	S 1.00000	39	77	Y	5	4	0	0	0	0	6	4
71-11	1	S 1.00000	39	78	NY	0	0	0	0	0	0	0	0
71-11	1	S 1.00000	40	79	Y	8	4	0	0	0	0	8	4
71-11	1	S 1.00000	40	80	Y	7	8	1	0	0	0	7	8
71-11	1	S 5.00000	41	81	Y	6	4	3	2	1	0	7	5
71-11	1	S 5.00000	41	82	YY	7	4	0	0	0	0	8	4
71-11	1	S 5.00000	42	83	Y	6	5	0	0	0	0	7	5
71-11	1	S 5.00000	42	84	YY	5	8	0	0	0	0	5	8
71-11	1	S 5.00000	43	85	YY	7	6	0	0	0	0	9	7
71-11	1	S 5.00000	43	86	Y	8	7	0	0	0	0	8	7
71-11	1	S 5.00000	44	87	YY	5	9	0	0	0	1	5	9
71-11	1	S 5.00000	44	88	Y	7	6	0	0	0	0	7	6
71-11	1	S 5.00000	45	89	YY	6	8	0	0	0	0	6	8
71-11	1	S 5.00000	45	90	Y	7	7	1	0	0	0	7	7
71-11	1	S 5.00000	46	91	Y	5	6	0	2	0	0	5	6
71-11	1	S 5.00000	46	92	YY	9	5	0	0	0	0	9	5
71-11	1	S 5.00000	47	93	YY	8	4	0	0	0	0	8	4
71-11	1	S 5.00000	47	94	Y	6	5	0	0	0	0	6	5
71-11	1	S 5.00000	48	95	YY	7	6	0	1	0	0	8	10
71-11	1	S 5.00000	48	96	YY	8	6	1	0	0	0	8	6
71-11	1	S 5.00000	49	97	Y	3	7	0	0	0	0	3	7
71-11	1	S 5.00000	49	98	YY	5	6	0	0	0	0	5	6
71-11	1	S 5.00000	50	99	Y	8	8	0	0	0	0	8	5
71-11	1	S 5.00000	50	100	Y	5	8	0	0	0	1	5	9

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SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORAL LUTEA	
								L	R	L	R	L	R
TEM	1	S	.00020	11	21	Y	6	5	0	0	0	0	8
TEM	1	S	.00020	11	22	Y	5	7	0	0	2	1	5
TEM	1	S	.00020	12	23	Y	5	4	0	0	0	0	4
TEM	1	S	.00020	12	24	Y	5	7	0	0	0	0	7
TEM	1	S	.00020	13	25	Y	9	5	2	1	0	0	5
TEM	1	S	.00020	13	26	Y	9	4	0	0	0	0	9
TEM	1	S	.00020	14	27	Y	5	6	0	0	0	0	6
TEM	1	S	.00020	14	28	Y	5	6	0	0	0	1	6
TEM	1	S	.00020	15	29	Y	6	7	0	0	0	0	7
TEM	1	S	.00020	15	30	Y	6	6	0	0	0	0	0
TEM	1	S	.00020	16	31	N	0	0	0	0	0	0	0
TEM	1	S	.00020	16	32	Y	8	6	0	0	0	0	3
TEM	1	S	.00020	17	33	Y	9	3	0	0	0	0	5
TEM	1	S	.00020	17	34	N	0	0	0	0	0	0	0
TEM	1	S	.00020	18	35	Y	4	5	0	0	0	0	1
TEM	1	S	.00020	18	36	Y	6	5	0	0	0	0	6
TEM	1	S	.00020	19	37	Y	7	5	3	2	0	0	9
TEM	1	S	.00020	19	38	Y	7	4	0	0	0	0	7
TEM	1	S	.00020	20	39	Y	6	8	0	0	0	0	1
TEM	1	S	.00020	20	40	N	0	0	0	0	0	0	0
CONTROL	1	M	0.00000	1	1	Y	8	4	1	0	0	0	10
CONTROL	1	M	0.00000	1	2	Y	8	5	0	0	0	0	8
CONTROL	1	M	0.00000	2	3	Y	3	6	1	0	1	0	3
CONTROL	1	M	0.00000	2	4	Y	3	6	2	0	1	0	4
CONTROL	1	M	0.00000	3	5	Y	3	9	1	0	0	0	9
CONTROL	1	M	0.00000	3	6	Y	4	7	1	0	0	0	3
CONTROL	1	M	0.00000	3	7	Y	5	7	2	0	0	0	5
CONTROL	1	M	0.00000	4	8	Y	5	7	2	0	0	0	5
CONTROL	1	M	0.00000	4	9	Y	7	5	2	0	0	0	7
CONTROL	1	M	0.00000	5	10	Y	10	4	0	0	0	0	11
CONTROL	1	M	0.00000	5	11	Y	4	8	0	0	0	0	4
CONTROL	1	M	0.00000	6	11	Y	5	5	1	0	0	0	4
CONTROL	1	M	0.00000	6	12	Y	5	7	1	0	0	0	7
CONTROL	1	M	0.00000	7	13	Y	4	9	0	0	0	0	4
CONTROL	1	M	0.00000	7	14	Y	7	7	1	0	0	0	7
CONTROL	1	M	0.00000	8	15	Y	4	6	0	0	0	0	5
CONTROL	1	M	0.00000	8	16	Y	7	5	2	0	0	0	7
CONTROL	1	M	0.00000	9	17	Y	6	4	0	0	0	0	6
CONTROL	1	M	0.00000	9	18	Y	10	0	0	0	0	0	10
CONTROL	1	M	0.00000	10	19	Y	0	3	0	0	0	0	4
CONTROL	1	M	0.00000	10	20	Y	3	8	0	0	0	0	3

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PRFG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
								L	R	L	R	L	R
71-11	1	M	.20000	11	21	Y	8	3	1	0	0	0	9
71-11	1	M	.20000	11	22	Y	3	7	0	1	0	0	3
71-11	1	M	.20000	12	23	Y	7	4	1	0	0	0	9
71-11	1	M	.20000	12	24	Y	4	8	0	0	0	0	4
71-11	1	M	.20000	13	25	Y	6	6	1	0	0	0	6
71-11	1	M	.20000	13	26	Y	7	6	1	0	0	0	7
71-11	1	M	.20000	14	27	Y	7	6	0	0	0	0	7
71-11	1	M	.20000	14	28	Y	7	7	1	0	0	0	8
71-11	1	M	.20000	15	29	Y	4	0	2	0	0	0	8
71-11	1	M	.20000	15	30	Y	3	8	0	1	0	0	3
71-11	1	M	.20000	16	31	Y	5	2	0	0	0	0	6
71-11	1	M	.20000	16	32	Y	3	9	0	0	0	0	3
71-11	1	M	.20000	17	33	N	0	0	0	0	0	0	0
71-11	1	M	.20000	17	34	Y	5	9	0	0	0	0	5
71-11	1	M	.20000	18	35	Y	8	5	0	1	0	0	9
71-11	1	M	.20000	18	36	Y	6	7	0	0	0	0	6
71-11	1	M	.20000	19	37	Y	6	4	0	0	1	0	5
71-11	1	M	.20000	19	38	Y	5	7	0	0	0	0	7
71-11	1	M	.20000	20	39	Y	3	9	0	1	0	0	3
71-11	1	M	.20000	20	40	Y	10	5	0	0	0	0	10
71-11	1	M	1.00000	21	41	Y	5	8	0	0	0	0	5
71-11	1	M	1.00000	21	42	N	0	0	0	0	0	0	0
71-11	1	M	1.00000	22	43	Y	7	6	0	0	0	0	7
71-11	1	M	1.00000	22	44	Y	0	0	0	0	0	0	0
71-11	1	M	1.00000	23	45	Y	9	4	0	0	0	0	9
71-11	1	M	1.00000	23	46	N	0	0	0	0	0	0	0
71-11	1	M	1.00000	24	47	N	0	0	0	0	0	0	0
71-11	1	M	1.00000	24	48	Y	7	6	0	1	4	0	7
71-11	1	M	1.00000	25	49	Y	0	7	0	0	0	0	4
71-11	1	M	1.00000	25	50	Y	0	0	0	0	0	0	0
71-11	1	M	1.00000	26	51	Y	5	8	0	1	4	1	5
71-11	1	M	1.00000	26	52	Y	6	4	0	0	0	0	6
71-11	1	M	1.00000	27	53	Y	0	0	0	0	0	0	0
71-11	1	M	1.00000	27	54	Y	5	8	0	0	0	0	5
71-11	1	M	1.00000	28	55	Y	13	2	0	0	0	0	13
71-11	1	M	1.00000	28	56	Y	5	6	0	0	0	0	2
71-11	1	M	1.00000	29	57	Y	6	5	0	0	0	0	6
71-11	1	M	1.00000	29	58	Y	7	5	0	1	1	0	7
71-11	1	M	1.00000	30	59	Y	10	4	1	1	0	0	10
71-11	1	M	1.00000	30	60	Y	4	8	0	0	0	0	5

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SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	R	L	R	L	R
71-11	1	M	5.00000	31	61	Y	3	6	0	0	0	0	3	7
71-11	1	M	5.00000	31	62	Y	3	7	0	0	0	1	5	8
71-11	1	M	5.00000	32	63	YY	6	5	0	0	0	0	6	5
71-11	1	M	5.00000	32	64	YY	6	4	0	0	0	0	7	4
71-11	1	M	5.00000	33	65	N	0	0	0	0	0	0	0	0
71-11	1	M	5.00000	33	66	YY	5	8	0	0	0	0	5	8
71-11	1	M	5.00000	34	67	YY	7	6	0	0	0	0	7	6
71-11	1	M	5.00000	34	68	YY	7	7	1	0	0	0	7	7
71-11	1	M	5.00000	35	69	YY	7	5	0	0	0	0	7	5
71-11	1	M	5.00000	35	70	YY	7	6	0	0	1	0	9	6
71-11	1	M	5.00000	36	71	YY	7	7	1	0	0	0	7	9
71-11	1	M	5.00000	36	72	N	0	0	0	0	0	0	0	0
71-11	1	M	5.00000	37	73	YY	7	3	0	0	0	0	7	3
71-11	1	M	5.00000	37	74	YY	8	4	2	0	0	1	8	4
71-11	1	M	5.00000	38	75	YY	7	4	0	1	0	0	8	4
71-11	1	M	5.00000	38	76	YY	10	2	0	0	0	0	10	2
71-11	1	M	5.00000	39	77	NN	0	0	0	0	0	0	0	0
71-11	1	M	5.00000	39	78	NN	0	0	0	0	0	0	0	0
71-11	1	M	5.00000	40	79	YY	3	3	2	0	0	0	6	4
71-11	1	M	5.00000	40	80	Y	5	7	0	0	0	0	6	7

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TEST MATERIAL	WEEK	S/M. DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
						L	R	L	R	L	R	L	R
CONTROL	2	S 0.00000	1	1	Y	5	6	0	1	0	0	5	7
CONTROL	2	S 0.00000	1	2	YY	5	7	0	0	0	0	5	7
CONTROL	2	S 0.00000	2	3	YY	1	6	0	0	0	0	6	6
CONTROL	2	S 0.00000	2	4	YY	3	6	0	1	0	0	3	8
CONTROL	2	S 0.00000	3	5	YY	6	6	0	0	0	0	6	6
CONTROL	2	S 0.00000	3	6	YY	5	5	0	0	0	0	5	7
CONTROL	2	S 0.00000	4	7	YY	6	4	0	0	0	0	6	4
CONTROL	2	S 0.00000	4	8	YY	5	7	0	0	0	0	5	7
CONTROL	2	S 0.00000	5	9	YY	2	5	0	0	1	1	6	5
CONTROL	2	S 0.00000	5	10	YY	4	8	0	0	1	1	5	8
CONTROL	2	S 0.00000	6	11	YY	4	6	0	0	0	0	5	6
CONTROL	2	S 0.00000	6	12	YY	4	5	0	0	0	0	4	6
CONTROL	2	S 0.00000	7	13	YY	6	8	0	0	0	0	7	8
CONTROL	2	S 0.00000	7	14	YY	7	6	0	0	0	0	7	6
CONTROL	2	S 0.00000	8	15	YY	1	9	0	0	0	0	12	12
CONTROL	2	S 0.00000	8	16	YY	6	6	0	0	0	0	6	6
CONTROL	2	S 0.00000	9	17	YY	5	7	0	0	0	0	6	7
CONTROL	2	S 0.00000	9	18	YY	5	7	1	0	0	1	5	9
CONTROL	2	S 0.00000	10	19	YY	7	6	0	0	0	0	7	9
CONTROL	2	S 0.00000	10	20	Y	2	5	0	0	0	0	3	9
71-11	2	S .20000	21	41	Y	7	6	0	1	0	0	7	6
71-11	2	S .20000	21	42	YY	6	6	0	0	0	0	6	7
71-11	2	S .20000	22	43	YY	8	5	1	0	0	0	8	5
71-11	2	S .20000	22	44	YY	4	7	0	0	0	0	8	8
71-11	2	S .20000	23	45	YY	6	7	0	0	0	0	6	7
71-11	2	S .20000	23	46	YY	5	6	0	0	0	0	7	6
71-11	2	S .20000	24	47	YY	7	5	0	0	0	0	4	4
71-11	2	S .20000	24	48	YY	1	1	1	1	0	0	5	11
71-11	2	S .20000	25	49	YY	4	10	0	0	0	0	7	9
71-11	2	S .20000	25	50	YY	6	9	0	0	2	4	8	7
71-11	2	S .20000	26	51	YY	8	7	0	0	0	0	8	9
71-11	2	S .20000	26	52	YY	4	6	0	0	1	0	10	5
71-11	2	S .20000	27	53	YY	9	7	1	0	0	0	7	8
71-11	2	S .20000	27	54	YY	4	8	1	0	0	0	4	7
71-11	2	S .20000	28	55	YY	4	7	0	0	0	1	0	0
71-11	2	S .20000	28	56	YY	6	5	0	0	0	0	0	0
71-11	2	S .20000	29	57	Y	0	0	0	0	1	0	0	0
71-11	2	S .20000	29	58	YY	5	7	0	0	0	0	5	7
71-11	2	S .20000	30	59	YY	6	9	0	0	0	0	7	6
71-11	2	S .20000	30	60	Y	6	6	0	0	0	0	0	6

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PHEG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA		
							L	R	L	R	L	R	L
71-11	2	S 1.00000	31	61	Y	2	9	0	0	1	0	5	9
71-11	2	S 1.00000	31	62	YY	6	7	0	0	0	0	7	8
71-11	2	S 1.00000	32	63	Y	8	2	0	0	0	0	9	3
71-11	2	S 1.00000	32	64	N	0	0	0	0	0	0	0	0
71-11	2	S 1.00000	33	65	Y	7	6	0	0	0	0	7	7
71-11	2	S 1.00000	33	66	YY	9	5	0	0	3	0	10	5
71-11	2	S 1.00000	34	67	Y	5	3	0	0	0	0	8	3
71-11	2	S 1.00000	34	68	YY	8	7	0	1	1	1	8	7
71-11	2	S 1.00000	35	69	Y	4	7	0	0	0	0	4	8
71-11	2	S 1.00000	35	70	YY	10	4	0	0	3	0	10	4
71-11	2	S 1.00000	36	71	Y	5	6	0	0	0	0	6	6
71-11	2	S 1.00000	36	72	YY	9	5	0	0	0	0	9	5
71-11	2	S 1.00000	37	73	Y	5	5	0	0	0	0	6	5
71-11	2	S 1.00000	37	74	YY	4	3	0	0	0	0	4	5
71-11	2	S 1.00000	38	75	Y	9	3	0	0	0	0	9	3
71-11	2	S 1.00000	38	76	YY	5	6	1	0	0	0	6	9
71-11	2	S 1.00000	39	77	Y	6	10	0	0	0	0	6	10
71-11	2	S 1.00000	39	78	YY	8	5	0	0	1	0	9	7
71-11	2	S 1.00000	40	79	Y	4	8	0	1	0	0	12	10
71-11	2	S 1.00000	40	80	Y	5	6	1	0	0	0	5	6
71-11	2	S 5.00000	41	81	Y	3	6	0	0	0	0	3	6
71-11	2	S 5.00000	41	82	YY	8	6	0	0	1	0	8	6
71-11	2	S 5.00000	42	83	Y	10	2	0	0	0	0	10	2
71-11	2	S 5.00000	42	84	YY	1	6	0	0	1	0	10	7
71-11	2	S 5.00000	43	85	Y	7	7	0	0	1	3	7	7
71-11	2	S 5.00000	43	86	YY	7	6	1	0	0	0	7	6
71-11	2	S 5.00000	44	87	Y	5	9	0	0	0	1	6	11
71-11	2	S 5.00000	44	88	YY	5	1	0	0	0	0	7	7
71-11	2	S 5.00000	45	89	Y	6	3	0	0	0	0	7	4
71-11	2	S 5.00000	45	90	Y	3	7	0	0	0	0	4	9
71-11	2	S 5.00000	46	91	Y	3	9	0	1	0	0	3	9
71-11	2	S 5.00000	46	92	YY	2	10	0	0	0	0	2	10
71-11	2	S 5.00000	47	93	Y	10	4	0	0	0	0	10	4
71-11	2	S 5.00000	47	94	YY	5	6	0	1	2	1	7	7
71-11	2	S 5.00000	48	95	Y	7	6	0	0	0	0	7	6
71-11	2	S 5.00000	48	96	YY	4	8	0	0	0	0	4	8
71-11	2	S 5.00000	49	97	Y	5	9	0	2	0	0	5	9
71-11	2	S 5.00000	49	98	YY	8	10	0	0	0	0	8	10
71-11	2	S 5.00000	50	99	Y	3	8	0	0	0	0	3	8
71-11	2	S 5.00000	50	100	Y	7	7	0	0	0	0	7	7

DOMINANT LETHAL STUDY OF COMPOUND 71-11

SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORAL LUTEA	
								L	R	L	R	L	R
TEM	2	S	.00020	11	21	Y	4	7	0	0	0	2	4
TEM	2	S	.00020	11	22	YY	7	4	4	1	0	0	7
TEM	2	S	.00020	12	23	YY	5	4	2	3	0	0	8
TEM	2	S	.00020	12	24	YY	6	5	0	0	0	0	5
TEM	2	S	.00020	13	25	YY	4	4	4	0	0	0	7
TEM	2	S	.00020	13	26	YY	4	9	1	7	0	0	5
TEM	2	S	.00020	14	27	YY	1	5	1	1	0	0	2
TEM	2	S	.00020	14	28	YY	1	5	2	0	0	0	4
TEM	2	S	.00020	15	29	YY	4	5	0	0	0	0	6
TEM	2	S	.00020	15	30	YY	4	7	4	6	0	0	4
TEM	2	S	.00020	16	31	YY	5	5	0	0	0	0	6
TEM	2	S	.00020	16	32	YY	4	3	4	3	0	0	7
TEM	2	S	.00020	17	33	YY	8	5	1	0	0	0	5
TEM	2	S	.00020	17	34	YY	5	4	4	3	0	0	5
TEM	2	S	.00020	18	35	YY	6	5	4	4	0	0	7
TEM	2	S	.00020	18	36	YY	6	4	3	3	0	0	6
TEM	2	S	.00020	19	37	YY	8	2	0	2	0	0	8
TEM	2	S	.00020	19	38	YY	8	2	2	6	0	0	7
TEM	2	S	.00020	20	39	YY	7	5	7	5	0	0	6
TEM	2	S	.00020	20	40	YY	2	6	2	4	0	0	7
CONTROL	2	M	0.00000	1	1	Y	3	10	0	1	0	0	3
CONTROL	2	M	0.00000	1	2	YY	5	8	0	0	0	0	5
CONTROL	2	M	0.00000	2	3	YY	7	6	1	0	0	0	6
CONTROL	2	M	0.00000	2	4	YY	4	7	0	0	0	0	4
CONTROL	2	M	0.00000	3	5	YY	6	5	1	1	0	0	7
CONTROL	2	M	0.00000	3	6	YY	9	3	0	1	0	0	5
CONTROL	2	M	0.00000	4	7	YY	6	7	1	0	0	0	6
CONTROL	2	M	0.00000	4	8	YY	5	7	0	0	0	0	5
CONTROL	2	M	0.00000	5	9	YY	8	7	0	0	0	0	8
CONTROL	2	M	0.00000	5	10	YY	8	7	0	0	0	0	7
CONTROL	2	M	0.00000	6	11	YY	8	7	0	0	0	0	8
CONTROL	2	M	0.00000	6	12	YY	4	8	0	1	0	0	5
CONTROL	2	M	0.00000	7	13	YY	8	6	2	0	0	0	8
CONTROL	2	M	0.00000	7	14	YY	7	5	1	1	0	0	8
CONTROL	2	M	0.00000	8	15	YY	6	7	0	0	0	0	6
CONTROL	2	M	0.00000	8	16	YY	6	6	0	0	0	0	6
CONTROL	2	M	0.00000	9	17	YY	8	5	1	1	0	0	9
CONTROL	2	M	0.00000	9	18	YY	5	5	0	0	0	0	5
CONTOL	2	M	0.00000	10	19	YY	7	1	0	0	0	0	2
CONTOL	2	M	0.00000	10	20	YY	12	0	0	0	0	0	12

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		COPROTA LUTEA		
								L	R	L	R	L	R	
71-11	2	M	.20000	11	21	Y	9	4	0	0	0	0	10	4
71-11	2	M	.20000	11	22	Y	4	5	1	0	0	0	4	6
71-11	2	M	.20000	12	23	Y	6	1	2	0	0	0	6	4
71-11	2	M	.20000	12	24	Y	6	7	0	1	0	0	6	7
71-11	2	M	.20000	13	25	Y	8	5	0	0	0	0	8	7
71-11	2	M	.20000	13	26	Y	6	4	0	0	0	0	6	5
71-11	2	M	.20000	14	27	Y	6	4	1	0	2	0	7	4
71-11	2	M	.20000	14	28	Y	9	3	0	0	2	2	9	4
71-11	2	M	.20000	15	29	Y	6	6	0	0	0	0	6	7
71-11	2	M	.20000	15	30	Y	7	5	0	0	0	0	7	5
71-11	2	M	.20000	16	31	Y	4	9	0	0	0	0	4	9
71-11	2	M	.20000	16	32	Y	6	7	0	0	0	0	8	7
71-11	2	M	.20000	17	33	Y	3	10	0	1	0	0	3	10
71-11	2	M	.20000	17	34	Y	5	5	0	0	0	0	5	6
71-11	2	M	.20000	18	35	Y	6	8	1	2	0	0	6	9
71-11	2	M	.20000	18	36	Y	3	10	0	1	0	1	3	10
71-11	2	M	.20000	19	37	Y	6	7	0	0	0	0	6	8
71-11	2	M	.20000	19	38	Y	6	5	1	0	0	0	6	7
71-11	2	M	.20000	20	39	Y	8	5	0	0	0	0	8	5
71-11	2	M	.20000	20	40	Y	5	6	0	0	0	1	6	7
71-11	2	M	1.00000	21	41	Y	7	6	0	0	0	0	7	6
71-11	2	M	1.00000	21	42	Y	8	4	0	0	0	0	8	5
71-11	2	M	1.00000	22	43	Y	4	7	0	0	0	0	4	7
71-11	2	M	1.00000	22	44	Y	7	0	0	0	0	0	7	7
71-11	2	M	1.00000	23	45	Y	4	9	0	0	0	0	4	9
71-11	2	M	1.00000	23	46	Y	9	4	1	0	0	0	10	5
71-11	2	M	1.00000	24	47	Y	9	6	0	0	0	0	5	7
71-11	2	M	1.00000	24	48	Y	5	4	0	0	0	0	5	4
71-11	2	M	1.00000	25	49	Y	8	7	0	0	0	1	8	8
71-11	2	M	1.00000	25	50	Y	7	5	0	0	0	0	7	7
71-11	2	M	1.00000	26	51	Y	7	6	1	0	0	0	7	6
71-11	2	M	1.00000	26	52	Y	6	6	0	0	0	0	7	6
71-11	2	M	1.00000	27	53	Y	6	6	0	1	0	1	10	7
71-11	2	M	1.00000	27	54	Y	9	6	0	0	0	0	10	5
71-11	2	M	1.00000	28	55	Y	9	4	1	0	0	0	10	6
71-11	2	M	1.00000	28	56	Y	9	6	0	0	0	1	10	6
71-11	2	M	1.00000	29	57	Y	8	6	0	0	0	1	7	6
71-11	2	M	1.00000	29	58	Y	6	6	0	0	0	0	7	6
71-11	2	M	1.00000	30	59	Y	7	6	0	0	0	0	7	6
71-11	2	M	1.00000	30	60	Y	4	8	0	0	0	0	4	8

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SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
						L	R	L	R	L	R	L	H
71-11	2	M 5.00000	31	61	Y	7	4	0	0	0	0	10	4
71-11	2	M 5.00000	31	62	Y	8	3	0	0	0	0	8	5
71-11	2	M 5.00000	32	63	Y	9	2	1	0	2	0	10	2
71-11	2	M 5.00000	32	64	Y	6	5	0	0	0	0	6	5
71-11	2	M 5.00000	33	65	Y	2	7	0	0	0	0	4	7
71-11	2	M 5.00000	33	66	Y	7	5	1	1	0	0	8	5
71-11	2	M 5.00000	34	67	Y	3	7	0	0	0	0	3	10
71-11	2	M 5.00000	34	68	Y	1	1	1	1	0	0	12	8
71-11	2	M 5.00000	35	69	Y	6	8	0	1	0	0	6	8
71-11	2	M 5.00000	35	70	Y	8	4	2	0	0	0	8	4
71-11	2	M 5.00000	36	71	Y	6	4	0	0	0	0	6	4
71-11	2	M 5.00000	36	72	Y	0	3	0	0	0	0	9	4
71-11	2	M 5.00000	37	73	Y	1	0	0	0	1	0	7	6
71-11	2	M 5.00000	37	74	Y	6	9	0	1	0	1	6	9
71-11	2	M 5.00000	38	75	Y	4	11	0	0	0	1	5	11
71-11	2	M 5.00000	38	76	Y	5	7	0	2	0	0	5	7
71-11	2	M 5.00000	39	77	Y	7	5	0	0	0	0	7	5
71-11	2	M 5.00000	39	78	Y	4	8	0	1	2	2	6	8
71-11	2	M 5.00000	40	79	Y	6	8	0	0	0	0	6	8
71-11	2	M 5.00000	40	80	Y	3	9	0	0	0	0	3	9

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
						L	R	L	R	L	R	L	R
CONTROL	3	S 0.00000	1	1	Y	7	5	1	0	0	0	8	5
CONTROL	3	S 0.00000	1	2	YY	3	7	0	2	0	0	4	9
CONTROL	3	S 0.00000	2	3	YY	4	10	0	0	0	0	4	10
CONTROL	3	S 0.00000	2	4	YY	3	10	0	0	0	0	4	10
CONTROL	3	S 0.00000	3	5	YY	5	7	0	0	0	0	5	9
CONTROL	3	S 0.00000	3	6	YY	11	3	0	0	0	0	11	3
CONTROL	3	S 0.00000	4	7	YY	7	3	0	0	0	0	7	4
CONTROL	3	S 0.00000	4	8	YY	8	5	0	0	0	0	8	6
CONTROL	3	S 0.00000	4	9	YY	5	7	0	0	0	0	5	7
CONTOL	3	S 0.00000	5	10	YY	8	2	0	0	0	0	8	3
CONTOL	3	S 0.00000	6	11	YY	9	5	0	0	1	1	9	6
CONTROL	3	S 0.00000	6	12	YY	5	7	0	1	0	0	5	7
CONTOL	3	S 0.00000	7	13	YY	5	7	0	0	0	0	5	5
CONTROL	3	S 0.00000	7	14	YY	5	5	0	0	0	0	5	5
CONTROL	3	S 0.00000	8	15	YY	7	4	4	2	0	0	7	4
CONTOL	3	S 0.00000	8	16	YY	7	6	0	0	0	0	7	6
CONTROL	3	S 0.00000	9	17	YY	8	6	0	0	0	0	8	6
CONTROL	3	S 0.00000	9	18	YY	6	4	0	1	0	1	6	4
CONTOL	3	S 0.00000	10	19	YY	9	4	0	0	0	0	9	4
CONTOL	3	S 0.00000	10	20	Y	7	9	0	0	0	2	7	9
71-11	3	S .20000	21	41	Y	1	0	0	0	0	0	5	7
71-11	3	S .20000	21	42	YY	5	5	0	2	0	0	5	5
71-11	3	S .20000	22	43	YY	6	8	0	0	0	0	6	8
71-11	3	S .20000	22	44	YY	7	5	0	0	1	0	9	5
71-11	3	S .20000	23	45	YY	2	8	0	0	0	0	2	9
71-11	3	S .20000	23	46	YY	6	5	0	0	0	0	6	6
71-11	3	S .20000	24	47	YY	5	8	0	0	0	0	5	8
71-11	3	S .20000	24	48	YY	7	5	0	1	0	0	7	6
71-11	3	S .20000	25	49	YY	7	6	0	0	0	0	7	7
71-11	3	S .20000	25	50	YY	5	5	0	0	0	0	5	7
71-11	3	S .20000	26	51	YY	8	7	1	0	0	0	8	7
71-11	3	S .20000	26	52	YY	8	5	0	0	1	0	8	5
71-11	3	S .20000	27	53	YY	7	5	0	1	0	0	9	5
71-11	3	S .20000	27	54	YY	7	5	0	0	1	0	8	7
71-11	3	S .20000	28	55	YY	4	10	0	0	0	1	4	10
71-11	3	S .20000	28	56	YY	9	5	0	0	0	1	9	5
71-11	3	S .20000	29	57	YY	6	7	0	0	1	0	7	7
71-11	3	S .20000	29	58	YY	7	7	0	0	1	0	7	7
71-11	3	S .20000	30	59	YY	7	6	0	0	0	0	7	6
71-11	3	S .20000	30	60	Y	2	9	0	0	0	0	3	9

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SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	R	L	R
71-11	3	S 1.00000	31	61	Y	8	4	1	0	0	0	10 4
71-11	3	S 1.00000	31	62	Y	5	7	2	0	0	0	5 7
71-11	3	S 1.00000	32	63	Y	8	5	0	0	0	0	9 5
71-11	3	S 1.00000	32	64	Y	9	7	1	0	0	0	9 7
71-11	3	S 1.00000	33	65	Y	5	7	0	0	0	0	5 7
71-11	3	S 1.00000	33	66	Y	8	6	0	0	0	0	9 6
71-11	3	S 1.00000	34	67	Y	6	7	0	0	0	1	7 7
71-11	3	S 1.00000	34	68	Y	7	7	1	0	0	0	7 8
71-11	3	S 1.00000	35	69	Y	7	7	1	0	0	0	7 7
71-11	3	S 1.00000	35	70	Y	5	5	0	0	1	0	5 6
71-11	3	S 1.00000	36	71	Y	8	4	0	0	0	0	9 4
71-11	3	S 1.00000	36	72	Y	4	2	0	0	0	0	5 8
71-11	3	S 1.00000	37	73	Y	4	7	0	0	0	1	4 8
71-11	3	S 1.00000	37	74	Y	3	8	0	0	0	0	3 8
71-11	3	S 1.00000	38	75	Y	6	8	1	1	0	0	6 8
71-11	3	S 1.00000	38	76	Y	8	5	0	0	0	0	8 5
71-11	3	S 1.00000	39	77	Y	6	6	0	0	0	0	6 6
71-11	3	S 1.00000	39	78	Y	10	3	0	0	0	0	10 3
71-11	3	S 1.00000	40	79	Y	5	7	0	0	0	0	6 7
71-11	3	S 1.00000	40	80	Y	5	8	1	0	0	0	5 9
71-11	3	S 5.00000	41	81	Y	4	10	0	0	0	0	4 11
71-11	3	S 5.00000	41	82	Y	3	7	0	0	0	0	3 8
71-11	3	S 5.00000	42	83	Y	3	10	0	0	0	1	3 12
71-11	3	S 5.00000	42	84	Y	4	8	0	0	0	1	4 8
71-11	3	S 5.00000	43	85	Y	6	5	0	0	0	0	6 5
71-11	3	S 5.00000	43	86	Y	5	7	0	0	0	0	5 7
71-11	3	S 5.00000	44	87	Y	5	8	0	0	0	0	5 8
71-11	3	S 5.00000	44	88	Y	3	9	0	0	1	0	3 9
71-11	3	S 5.00000	45	89	Y	9	5	0	0	0	0	9 5
71-11	3	S 5.00000	45	90	Y	6	4	0	0	0	0	7 4
71-11	3	S 5.00000	46	91	Y	3	10	0	0	0	0	3 10
71-11	3	S 5.00000	46	92	Y	6	5	0	0	0	0	6 5
71-11	3	S 5.00000	47	93	Y	9	4	0	0	0	0	9 4
71-11	3	S 5.00000	47	94	Y	8	4	1	0	0	0	7 6
71-11	3	S 5.00000	48	95	Y	6	5	0	0	0	0	7 6
71-11	3	S 5.00000	48	96	Y	6	7	1	0	0	0	6 7
71-11	3	S 5.00000	49	97	Y	7	5	0	0	0	0	7 6
71-11	3	S 5.00000	49	98	Y	8	4	0	0	0	0	9 4
71-11	3	S 5.00000	50	99	Y	7	7	0	0	0	0	7 7
71-11	3	S 5.00000	50	100	Y	6	7	1	1	0	0	7 8

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PHEG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	H	L	R
TEM	3	S .00020	11	21	Y	5	3	4	3	0	0	7 3
TEM	3	S .00020	11	22	YY	4	2	4	2	0	0	7 2
TEM	3	S .00020	12	23	YY	3	7	0	0	0	0	5 8
TEM	3	S .00020	12	24	YY	6	5	6	4	0	0	7 6
TEM	3	S .00020	13	25	YY	0	2	0	2	1	0	5 7
TEM	3	S .00020	13	26	YY	8	4	6	2	0	0	8 5
TEM	3	S .00020	14	27	YY	4	5	4	5	0	0	5 6
TEM	3	S .00020	14	28	YY	1	2	2	4	0	0	7 6
TEM	3	S .00020	15	29	YY	3	4	2	5	1	0	4 4
TEM	3	S .00020	15	30	YY	4	6	2	5	0	0	5 7
TEM	3	S .00020	16	31	YY	4	5	4	5	0	0	4 7
TEM	3	S .00020	16	32	YY	5	3	5	3	0	0	5 4
TEM	3	S .00020	17	33	YY	0	1	0	1	0	0	4 7
TEM	3	S .00020	17	34	YY	3	2	3	2	0	0	3 3
TEM	3	S .00020	18	35	YY	4	5	4	5	0	0	6 5
TEM	3	S .00020	18	36	YY	2	1	2	1	0	0	7 6
TEM	3	S .00020	19	37	YY	3	4	2	2	0	0	7 6
TEM	3	S .00020	19	38	YY	5	5	5	5	0	0	5 5
TEM	3	S .00020	20	39	YY	4	2	4	2	0	0	6 5
TEM	3	S .00020	20	40	Y	3	8	2	4	0	1	3 9
CONTROL	3	M 0.00000	1	1	YY	3	0	0	0	0	0	3 8
CONTROL	3	M 0.00000	1	2	YY	5	8	0	0	0	0	5 8
CONTOL	3	M 0.00000	2	3	YY	7	5	0	0	0	0	7 5
CONTROL	3	M 0.00000	2	4	YY	7	8	0	0	0	0	7 8
CONTROL	3	M 0.00000	3	5	YY	6	0	1	0	0	0	6 4
CONTROL	3	M 0.00000	3	6	YY	10	3	1	0	0	0	10 3
CONTROL	3	M 0.00000	4	7	YY	7	6	0	0	0	0	8 6
CONTROL	3	M 0.00000	4	8	YY	6	7	0	0	0	0	6 7
CONTROL	3	M 0.00000	5	9	YY	10	3	3	2	0	0	10 4
CONTROL	3	M 0.00000	5	10	YY	4	9	0	1	0	0	5 9
CONTROL	3	M 0.00000	6	11	YY	3	9	0	0	1	2	3 9
CONTROL	3	M 0.00000	6	12	YY	4	5	2	0	0	0	5 6
CONTROL	3	M 0.00000	7	13	YY	5	7	0	0	0	0	6 8
CONTROL	3	M 0.00000	7	14	YY	6	8	0	0	0	0	7 5
CONTROL	3	M 0.00000	8	15	YY	7	4	0	0	0	0	7 5
CONTROL	3	M 0.00000	8	16	YY	7	5	0	0	0	0	7 6
CONTROL	3	M 0.00000	9	17	YY	5	9	0	0	1	0	10 4
CONTROL	3	M 0.00000	9	18	YY	7	6	0	1	0	1	7 6
CONTROL	3	M 0.00000	10	19	YY	10	4	1	1	0	1	10 4
CONTROL	3	M 0.00000	10	20	Y	6	4	0	0	0	0	8 4

DOMINANT LETHAL STUDY OF COMPOUND 71-11

SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		COMPOUND LUTEA	
							L	R	L	R	L	R	L	R
71-11	3	M	.20000	11	21	Y	7	6	0	0	0	0	7	8
71-11	3	M	.20000	11	22	Y	2	9	0	0	0	0	4	9
71-11	3	M	.20000	12	23	Y	5	6	0	0	1	0	5	7
71-11	3	M	.20000	12	24	Y	4	7	0	0	1	0	4	7
71-11	3	M	.20000	13	25	Y	7	3	0	0	0	0	7	3
71-11	3	M	.20000	13	26	Y	6	6	0	0	0	0	6	6
71-11	3	M	.20000	14	27	Y	4	6	0	0	0	0	4	6
71-11	3	M	.20000	14	28	Y	1	1	0	0	0	0	3	1
71-11	3	M	.20000	15	29	Y	6	5	0	0	0	0	8	6
71-11	3	M	.20000	15	30	Y	6	6	0	0	0	0	6	6
71-11	3	M	.20000	16	31	Y	9	5	1	0	0	0	9	5
71-11	3	M	.20000	16	32	Y	6	8	0	0	0	0	6	9
71-11	3	M	.20000	17	33	Y	5	7	0	0	0	0	5	7
71-11	3	M	.20000	17	34	Y	1	0	1	0	0	0	8	12
71-11	3	M	.20000	18	35	Y	1	13	1	0	0	0	4	13
71-11	3	M	.20000	18	36	Y	6	8	0	0	0	0	7	11
71-11	3	M	.20000	19	37	Y	5	11	0	0	1	0	5	11
71-11	3	M	.20000	19	38	Y	5	9	0	0	0	0	5	9
71-11	3	M	.20000	20	39	Y	5	9	0	0	0	0	6	9
71-11	3	M	.20000	20	40	Y	4	10	0	0	1	1	4	11
71-11	3	M	1.00000	21	41	Y	6	4	0	0	0	0	6	4
71-11	3	M	1.00000	21	42	Y	8	5	0	0	0	0	8	5
71-11	3	M	1.00000	22	43	Y	3	7	0	0	0	0	3	7
71-11	3	M	1.00000	22	44	Y	2	3	1	1	0	0	9	9
71-11	3	M	1.00000	23	45	Y	7	6	0	1	0	0	7	6
71-11	3	M	1.00000	23	46	Y	6	8	0	1	0	0	8	9
71-11	3	M	1.00000	24	47	Y	7	8	0	1	0	0	4	8
71-11	3	M	1.00000	24	48	Y	4	8	0	0	0	0	7	7
71-11	3	M	1.00000	25	49	Y	6	7	0	0	0	0	7	7
71-11	3	M	1.00000	25	50	Y	7	7	0	0	0	0	5	8
71-11	3	M	1.00000	26	51	Y	5	6	1	2	0	0	11	4
71-11	3	M	1.00000	26	52	Y	11	4	0	0	0	0	9	5
71-11	3	M	1.00000	27	53	Y	9	5	0	1	0	0	4	7
71-11	3	M	1.00000	27	54	Y	4	7	0	1	0	0	8	8
71-11	3	M	1.00000	28	55	Y	8	8	0	0	0	0	6	5
71-11	3	M	1.00000	28	56	Y	5	5	0	0	0	0	6	7
71-11	3	M	1.00000	29	57	Y	6	6	0	0	0	0	9	5
71-11	3	M	1.00000	29	58	Y	9	5	0	0	0	0	5	5
71-11	3	M	1.00000	30	59	Y	5	5	0	0	0	0	5	7
71-11	3	M	1.00000	30	60	Y	5	5	0	0	0	0	0	0

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SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
						L	R	L	R	L	R	L	R
71-11	3	M 5.00000	31	61	Y	6	9	0	0	0	0	6	10
71-11	3	M 5.00000	31	62	Y	6	7	0	0	0	0	6	8
71-11	3	M 5.00000	32	63	Y	6	7	0	0	1	0	6	7
71-11	3	M 5.00000	32	64	YY	7	7	3	1	0	0	8	7
71-11	3	M 5.00000	33	65	YY	7	4	0	0	0	0	7	4
71-11	3	M 5.00000	33	66	YY	3	9	0	0	0	0	3	9
71-11	3	M 5.00000	34	67	YY	8	6	0	0	0	0	10	6
71-11	3	M 5.00000	34	68	YY	7	6	0	1	2	2	7	6
71-11	3	M 5.00000	35	69	YY	4	8	0	0	0	1	4	8
71-11	3	M 5.00000	35	70	YY	7	3	0	0	0	1	8	4
71-11	3	M 5.00000	36	71	YY	6	6	0	0	1	0	6	6
71-11	3	M 5.00000	36	72	YY	5	5	0	1	0	0	5	5
71-11	3	M 5.00000	37	73	YY	6	8	0	0	0	0	6	8
71-11	3	M 5.00000	37	74	YY	5	8	1	0	0	0	5	9
71-11	3	M 5.00000	38	75	YY	4	5	0	1	0	0	4	5
71-11	3	M 5.00000	38	76	YY	5	8	2	0	0	0	5	8
71-11	3	M 5.00000	39	77	YY	4	7	0	0	1	1	8	4
71-11	3	M 5.00000	39	78	YY	8	3	0	1	0	0	8	4
71-11	3	M 5.00000	40	79	YY	4	7	1	0	0	0	4	7
71-11	3	M 5.00000	40	80	Y	6	8	0	0	0	0	6	8

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SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA		
							L	R	L	R	L	R	L
CONTROL	4	S 0.00000	1	1	Y	7	4	0	0	0	0	7	5
CONTROL	4	S 0.00000	1	2	YY	4	6	0	0	0	0	5	6
CONTROL	4	S 0.00000	2	3	YY	8	5	0	0	0	1	8	6
CONTROL	4	S 0.00000	2	4	YY	5	9	0	1	0	0	5	9
CONTROL	4	S 0.00000	3	5	Y	7	7	0	0	0	0	8	7
CONTROL	4	S 0.00000	3	6	YY	6	4	0	0	0	0	6	4
CONTROL	4	S 0.00000	4	7	YY	5	8	0	0	0	0	8	8
CONTROL	4	S 0.00000	4	8	Y	8	8	0	0	0	0	7	6
CONTROL	4	S 0.00000	5	9	Y	7	6	0	1	0	0	6	9
CONTROL	4	S 0.00000	5	10	YY	4	8	0	0	0	0	6	9
CONTROL	4	S 0.00000	6	11	YY	1	3	0	0	0	0	4	5
CONTROL	4	S 0.00000	6	12	YY	4	9	0	1	0	0	4	9
CONTROL	4	S 0.00000	7	13	Y	7	8	0	1	0	0	7	8
CONTROL	4	S 0.00000	7	14	YY	7	5	1	0	0	0	7	5
CONTROL	4	S 0.00000	8	15	YY	10	3	0	2	0	0	10	4
CONTROL	4	S 0.00000	8	16	YY	3	8	0	0	0	0	3	8
CONTROL	4	S 0.00000	9	17	YY	4	7	0	1	0	0	4	7
CONTROL	4	S 0.00000	9	18	YY	5	4	0	0	0	0	5	4
CONTROL	4	S 0.00000	10	19	YY	3	9	0	0	0	0	3	9
CONTROL	4	S 0.00000	10	20	Y	6	5	0	0	0	0	6	5
71-11	4	S .20000	21	41	Y	5	7	4	1	0	0	7	8
71-11	4	S .20000	21	42	Y	6	4	0	0	0	0	6	4
71-11	4	S .20000	22	43	YY	8	4	1	0	2	0	8	5
71-11	4	S .20000	22	44	YY	5	6	0	1	0	0	5	7
71-11	4	S .20000	23	45	Y	8	4	1	0	0	0	8	4
71-11	4	S .20000	23	46	YY	9	6	0	0	0	1	10	6
71-11	4	S .20000	24	47	YY	6	6	0	3	0	0	6	6
71-11	4	S .20000	24	48	YY	6	6	0	0	0	0	6	6
71-11	4	S .20000	25	49	YY	7	7	0	0	0	0	7	7
71-11	4	S .20000	25	50	YY	5	7	0	0	0	1	5	7
71-11	4	S .20000	26	51	YY	6	6	0	0	0	0	6	7
71-11	4	S .20000	26	52	YY	2	11	1	0	0	0	2	11
71-11	4	S .20000	27	53	YY	2	8	0	1	0	0	2	10
71-11	4	S .20000	27	54	YY	4	0	0	0	0	0	4	7
71-11	4	S .20000	28	55	YY	7	5	1	0	0	1	7	5
71-11	4	S .20000	28	56	YY	6	6	3	0	0	0	6	6
71-11	4	S .20000	29	57	YY	7	7	0	0	0	0	7	7
71-11	4	S .20000	29	58	YY	4	6	0	0	0	0	5	9
71-11	4	S .20000	30	59	YY	5	9	0	0	0	0	5	8
71-11	4	S .20000	30	60	Y	6	7	0	0	0	0	7	8

DOMINANT LETHAL STUDY OF COMPOUND 71-11

SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		COMPORA LUTEA		
							L	R	L	R	L	R	
71-11	4	S 1.00000	31	61	Y	1	7	0	0	0	1	1	8
71-11	4	S 1.00000	31	62	Y	7	3	0	0	0	0	7	3
71-11	4	S 1.00000	32	63	Y	5	8	0	0	1	0	5	9
71-11	4	S 1.00000	32	64	Y	6	6	0	0	0	0	6	7
71-11	4	S 1.00000	33	65	Y	6	8	0	1	0	0	6	8
71-11	4	S 1.00000	33	66	Y	7	4	0	0	0	0	7	4
71-11	4	S 1.00000	34	67	Y	6	7	2	3	1	1	6	13
71-11	4	S 1.00000	34	68	Y	6	6	0	1	0	0	6	6
71-11	4	S 1.00000	35	69	Y	4	9	0	0	0	0	5	10
71-11	4	S 1.00000	35	70	Y	2	8	0	0	0	0	2	8
71-11	4	S 1.00000	36	71	Y	4	6	1	0	0	1	5	6
71-11	4	S 1.00000	36	72	Y	7	4	0	0	0	0	7	4
71-11	4	S 1.00000	37	73	Y	6	4	0	0	0	0	6	4
71-11	4	S 1.00000	37	74	Y	3	8	0	0	0	0	3	8
71-11	4	S 1.00000	38	75	Y	9	7	0	0	0	0	9	7
71-11	4	S 1.00000	38	76	Y	8	4	0	0	0	0	8	6
71-11	4	S 1.00000	39	77	Y	4	7	0	1	0	0	4	9
71-11	4	S 1.00000	39	78	Y	4	6	0	0	0	0	5	6
71-11	4	S 1.00000	40	79	Y	3	7	0	1	0	0	4	7
71-11	4	S 1.00000	40	80	N	0	0	0	0	0	0	0	0
71-11	4	S 5.00000	41	81	Y	9	4	0	3	0	0	9	4
71-11	4	S 5.00000	41	82	Y	7	4	0	0	0	0	7	4
71-11	4	S 5.00000	42	83	Y	9	5	1	0	0	0	10	5
71-11	4	S 5.00000	42	84	Y	6	7	0	0	0	0	6	7
71-11	4	S 5.00000	43	85	Y	6	3	1	0	0	0	6	4
71-11	4	S 5.00000	43	86	Y	8	5	2	0	0	0	8	6
71-11	4	S 5.00000	44	87	Y	4	9	0	0	0	0	4	9
71-11	4	S 5.00000	44	88	Y	5	6	1	0	0	0	6	6
71-11	4	S 5.00000	45	89	Y	7	8	0	1	0	0	7	8
71-11	4	S 5.00000	45	90	Y	4	7	0	0	0	0	5	7
71-11	4	S 5.00000	46	91	Y	7	6	1	1	1	0	7	6
71-11	4	S 5.00000	46	92	Y	7	8	0	5	4	0	7	8
71-11	4	S 5.00000	47	93	Y	8	5	0	0	0	1	8	5
71-11	4	S 5.00000	47	94	Y	7	6	0	0	0	0	8	6
71-11	4	S 5.00000	48	95	Y	6	4	0	0	0	0	10	5
71-11	4	S 5.00000	48	96	Y	4	12	0	1	0	0	4	12
71-11	4	S 5.00000	49	97	Y	6	6	0	1	0	0	6	6
71-11	4	S 5.00000	49	98	Y	4	8	0	0	1	0	4	9
71-11	4	S 5.00000	50	99	Y	10	6	0	1	0	0	10	7
71-11	4	S 5.00000	50	100	Y	6	6	0	0	0	0	6	6

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA		
								L	R	L	R	L	R	
TEM	4	S	.00020	11	21	Y	6	7	4	1	0	1	7	7
TEM	4	S	.00020	11	22	YY	1	3	1	3	0	0	9	9
TEM	4	S	.00020	12	23	Y	2	2	2	2	0	0	8	4
TEM	4	S	.00020	12	24	Y	4	8	0	0	4	8	5	8
TEM	4	S	.00020	13	25	YY	0	2	0	2	0	0	4	6
TEM	4	S	.00020	13	26	YY	3	3	3	3	0	0	9	5
TEM	4	S	.00020	14	27	YY	0	0	0	2	0	0	0	0
TEM	4	S	.00020	14	28	YY	0	2	3	2	0	0	5	6
TEM	4	S	.00020	15	29	YY	3	2	3	2	2	0	5	6
TEM	4	S	.00020	15	30	Y	2	3	2	2	2	0	5	8
TEM	4	S	.00020	16	31	N	0	0	0	0	0	0	0	0
TEM	4	S	.00020	16	32	YY	5	3	4	3	0	0	8	3
TEM	4	S	.00020	17	33	YY	1	1	1	1	0	0	4	3
TEM	4	S	.00020	17	34	YY	5	5	5	5	0	0	8	6
TEM	4	S	.00020	18	35	YY	2	2	2	4	0	0	5	8
TEM	4	S	.00020	18	36	YY	2	1	2	1	0	0	6	4
TEM	4	S	.00020	19	37	Y	0	0	0	0	0	0	0	0
TEM	4	S	.00020	19	38	YY	2	4	1	4	0	0	4	7
TEM	4	S	.00020	20	39	YY	3	5	3	5	0	0	5	7
TEM	4	S	.00020	20	40	Y	4	3	3	2	0	0	6	5
CONTROL	4	M	0.00000	1	1	YY	7	4	0	0	1	2	8	4
CONTROL	4	M	0.00000	1	2	YY	0	1	0	0	0	0	6	6
CONTROL	4	M	0.00000	2	3	YY	7	3	0	0	0	2	7	4
CONTROL	4	M	0.00000	2	4	YY	3	0	1	0	0	0	5	5
CONTROL	4	M	0.00000	3	5	YY	10	6	0	0	1	0	10	6
CONTROL	4	M	0.00000	3	6	YY	5	7	0	0	0	0	5	7
CONTROL	4	M	0.00000	3	6	YY	8	5	0	0	0	0	8	5
CONTROL	4	M	0.00000	4	7	YY	7	4	2	0	0	0	8	4
CONTROL	4	M	0.00000	4	8	YY	7	7	0	0	0	0	7	7
CONTROL	4	M	0.00000	5	9	YY	7	7	0	0	0	0	4	9
CONTROL	4	M	0.00000	5	10	YY	4	9	0	0	0	0	6	8
CONTROL	4	M	0.00000	6	11	Y	5	8	0	0	0	1	6	8
CONTROL	4	M	0.00000	6	12	YY	5	7	0	0	1	2	6	7
CONTROL	4	M	0.00000	7	13	YY	8	7	0	0	0	0	12	9
CONTROL	4	M	0.00000	7	14	YY	9	7	1	0	0	2	4	7
CONTROL	4	M	0.00000	8	15	YY	10	5	1	0	0	1	10	5
CONTROL	4	M	0.00000	8	16	YY	5	9	1	0	0	0	6	10
CONTROL	4	M	0.00000	9	17	YY	11	4	2	0	0	0	14	5
CONTROL	4	M	0.00000	9	18	YY	8	13	0	0	0	0	10	13
CONTROL	4	M	0.00000	10	19	YY	5	6	1	2	0	0	7	6
CONTROL	4	M	0.00000	10	20	Y	2	10	0	0	0	0	7	14

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SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA		
								L	H	L	H	L	H	
71-11	4	M	.20000	11	21	Y	5	9	1	0	0	0	6	9
71-11	4	M	.20000	11	22	YY	7	7	0	0	0	0	7	7
71-11	4	M	.20000	12	23	YY	10	4	0	0	0	0	11	5
71-11	4	M	.20000	12	24	YY	6	10	0	2	0	0	6	10
71-11	4	M	.20000	13	25	YY	4	7	0	0	0	0	5	9
71-11	4	M	.20000	13	26	YY	5	9	0	0	0	0	5	9
71-11	4	M	.20000	14	27	YY	7	8	1	1	0	0	7	8
71-11	4	M	.20000	14	28	YY	8	5	1	0	0	0	8	5
71-11	4	M	.20000	15	29	YY	5	5	0	1	0	0	6	5
71-11	4	M	.20000	15	30	YY	12	3	0	0	0	0	12	4
71-11	4	M	.20000	16	31	YY	5	7	0	0	0	0	6	9
71-11	4	M	.20000	16	32	YY	4	8	0	1	0	0	10	13
71-11	4	M	.20000	17	33	YY	9	10	0	0	0	0	9	10
71-11	4	M	.20000	17	34	YY	6	6	0	0	0	0	6	8
71-11	4	M	.20000	18	35	YY	10	2	0	0	0	0	10	2
71-11	4	M	.20000	18	36	YY	6	9	0	0	0	0	6	9
71-11	4	M	.20000	19	37	YY	6	6	0	0	0	0	6	7
71-11	4	M	.20000	19	38	YY	5	7	0	0	0	0	5	7
71-11	4	M	.20000	20	39	YY	4	5	0	0	0	0	4	8
71-11	4	M	.20000	20	40	Y	4	7	0	0	0	0	4	H
71-11	4	M	1.00000	21	41	YY	4	9	1	0	0	0	4	9
71-11	4	M	1.00000	21	42	YY	9	6	1	0	0	0	9	7
71-11	4	M	1.00000	22	43	YY	5	7	0	0	0	0	5	7
71-11	4	M	1.00000	22	44	YY	10	7	0	0	0	0	10	7
71-11	4	M	1.00000	23	45	YY	8	4	0	0	0	0	8	5
71-11	4	M	1.00000	23	46	YY	8	5	0	0	1	0	8	5
71-11	4	M	1.00000	24	47	YY	5	9	1	0	0	1	5	9
71-11	4	M	1.00000	24	48	YY	0	4	0	0	0	0	5	6
71-11	4	M	1.00000	25	49	YY	7	7	1	0	0	0	7	7
71-11	4	M	1.00000	25	50	YY	8	7	1	0	0	0	8	8
71-11	4	M	1.00000	26	51	YY	6	7	0	0	0	0	6	7
71-11	4	M	1.00000	26	52	YY	10	5	0	1	3	1	10	5
71-11	4	M	1.00000	27	53	YY	6	8	1	0	0	0	6	8
71-11	4	M	1.00000	27	54	YY	7	9	0	1	0	0	7	9
71-11	4	M	1.00000	28	55	YY	7	7	0	0	0	0	7	7
71-11	4	M	1.00000	28	56	YY	8	8	0	0	0	0	8	8
71-11	4	M	1.00000	29	57	YY	7	6	0	1	0	0	8	6
71-11	4	M	1.00000	29	58	YY	5	9	0	0	0	0	6	9
71-11	4	M	1.00000	30	59	YY	4	9	0	0	0	0	6	9
71-11	4	M	1.00000	30	60	Y	4	1	1	0	0	0	8	5

DOMINANT LETHAL STUDY OF COMPOUND 71-11

SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		COMPOUNA LUTEA	
							L	R	L	R	L	R
71-11	4	M 5.00000	31	61	Y	3	12	0	0	0	0	3 12
71-11	4	M 5.00000	31	62	N	0	0	0	0	0	0	0 0
71-11	4	M 5.00000	32	63	YY	6	8	2	0	0	0	6 9
71-11	4	M 5.00000	32	64	YY	5	6	1	0	0	0	8 6
71-11	4	M 5.00000	33	65	N	0	0	0	0	0	0	0 0
71-11	4	M 5.00000	33	66	YY	5	10	0	1	0	0	5 10
71-11	4	M 5.00000	34	67	YY	9	6	0	0	0	0	9 6
71-11	4	M 5.00000	34	68	YY	11	4	0	0	0	0	11 4
71-11	4	M 5.00000	35	69	YY	7	7	0	0	0	0	7 7
71-11	4	M 5.00000	35	70	YY	8	7	1	1	0	0	8 7
71-11	4	M 5.00000	36	71	YY	7	3	0	0	0	0	7 3
71-11	4	M 5.00000	36	72	YY	8	9	1	0	0	0	8 9
71-11	4	M 5.00000	37	73	YY	6	9	0	0	0	0	6 9
71-11	4	M 5.00000	37	74	YY	7	7	0	1	0	0	9 7
71-11	4	M 5.00000	38	75	YY	4	9	0	0	0	0	4 10
71-11	4	M 5.00000	38	76	YY	8	6	1	0	0	0	8 6
71-11	4	M 5.00000	39	77	YY	7	9	0	0	0	0	7 9
71-11	4	M 5.00000	39	78	YY	5	6	0	0	0	0	6 7
71-11	4	M 5.00000	40	79	YY	5	8	1	0	0	0	5 8
71-11	4	M 5.00000	40	80	Y	1	5	1	5	0	0	6 5

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SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		COMPORA LUTEA	
							L	R	L	R	L	H
CONTROL	5	S 0.00000	1	1	Y	5	9	2	1	0	0	6
CONTROL	5	S 0.00000	1	2	Y	4	2	0	0	0	0	6
CONTROL	5	S 0.00000	2	3	Y	9	6	0	0	0	0	6
CNTROL	5	S 0.00000	2	4	Y	5	10	0	0	0	1	5
CONTROL	5	S 0.00000	3	5	Y	8	5	0	0	0	0	6
CONTOL	5	S 0.00000	3	6	Y	5	9	0	0	0	0	5
CONTROL	5	S 0.00000	4	7	Y	4	11	0	0	0	0	11
CONTROL	5	S 0.00000	4	8	Y	5	8	0	1	0	1	5
CONTROL	5	S 0.00000	5	9	Y	7	3	0	0	0	0	4
CONTROL	5	S 0.00000	5	10	Y	7	6	0	1	0	0	6
CONTROL	5	S 0.00000	6	11	Y	8	4	0	0	0	0	4
CONTROL	5	S 0.00000	6	12	Y	5	8	0	0	1	3	10
CONTROL	5	S 0.00000	7	13	Y	4	9	0	0	0	0	10
CONTROL	5	S 0.00000	7	14	Y	7	7	0	1	0	0	7
CONTROL	5	S 0.00000	8	15	Y	3	8	0	0	0	1	9
CONTOL	5	S 0.00000	8	16	Y	7	7	1	1	0	0	7
CONTROL	5	S 0.00000	9	17	Y	5	10	1	0	0	0	10
CONTROL	5	S 0.00000	9	18	Y	1	6	0	0	0	0	8
CONTROL	5	S 0.00000	9	19	Y	6	5	1	2	0	0	6
CONTROL	5	S 0.00000	10	20	Y	7	7	2	2	0	0	7
71-11	5	S .20000	21	41	Y	3	11	0	0	0	0	12
71-11	5	S .20000	21	42	Y	4	7	0	0	0	0	7
71-11	5	S .20000	22	43	Y	6	8	2	0	0	0	8
71-11	5	S .20000	22	44	YY	6	4	0	0	0	0	4
71-11	5	S .20000	23	45	YY	7	5	0	0	0	0	5
71-11	5	S .20000	23	46	YY	6	10	0	0	0	0	10
71-11	5	S .20000	24	47	YY	5	7	0	0	0	0	7
71-11	5	S .20000	24	48	YY	5	8	0	0	0	0	8
71-11	5	S .20000	25	49	YY	5	10	0	0	0	0	11
71-11	5	S .20000	25	50	YY	3	12	0	0	2	3	12
71-11	5	S .20000	26	51	YY	8	4	0	0	0	1	8
71-11	5	S .20000	26	52	YY	7	6	0	0	0	0	6
71-11	5	S .20000	27	53	YY	7	9	0	0	0	0	9
71-11	5	S .20000	27	54	YY	6	8	0	1	0	0	8
71-11	5	S .20000	28	55	YY	7	6	1	0	1	0	6
71-11	5	S .20000	28	56	YY	6	7	1	1	0	0	7
71-11	5	S .20000	29	57	YY	6	15	0	0	0	0	7
71-11	5	S .20000	29	58	YY	7	5	2	1	0	0	6
71-11	5	S .20000	30	59	YY	8	9	0	0	0	0	5
71-11	5	S .20000	30	60	YY	4	9	0	0	0	0	9

DOMINANT LETHAL STUDY OF COMPOUND 71-11

SODIUM SACCHARIN

PAGE ??

TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA		
							L	R	L	R	L	R	
71-11	5	S 1.00000	31	61	Y	5	9	1	0	0	0	5	9
71-11	5	S 1.00000	31	62	Y	6	7	0	0	0	0	6	7
71-11	5	S 1.00000	32	63	Y	4	9	0	0	0	0	4	9
71-11	5	S 1.00000	32	64	Y	5	7	0	0	0	0	5	8
71-11	5	S 1.00000	33	65	Y	6	8	0	0	0	0	6	8
71-11	5	S 1.00000	33	66	Y	9	6	0	0	0	0	9	6
71-11	5	S 1.00000	34	67	Y	6	7	0	0	0	0	6	8
71-11	5	S 1.00000	34	68	Y	8	5	0	0	0	0	8	6
71-11	5	S 1.00000	35	69	Y	6	7	0	1	0	0	6	7
71-11	5	S 1.00000	35	70	Y	9	3	0	0	0	0	9	3
71-11	5	S 1.00000	36	71	Y	5	6	0	0	0	0	5	7
71-11	5	S 1.00000	36	72	Y	8	6	0	0	0	0	9	6
71-11	5	S 1.00000	37	73	Y	9	2	0	0	0	0	9	2
71-11	5	S 1.00000	37	74	Y	7	7	1	1	0	0	8	7
71-11	5	S 1.00000	38	75	Y	10	1	0	0	1	0	10	2
71-11	5	S 1.00000	38	76	Y	8	5	1	0	0	0	9	6
71-11	5	S 1.00000	39	77	Y	7	6	0	0	0	0	7	6
71-11	5	S 1.00000	39	78	Y	5	6	1	1	0	0	5	6
71-11	5	S 1.00000	40	79	Y	5	6	0	1	0	1	7	6
71-11	5	S 1.00000	40	80	Y	8	8	1	0	0	0	8	8
71-11	5	S 5.00000	41	81	Y	6	7	0	0	0	0	7	7
71-11	5	S 5.00000	41	82	Y	8	7	0	0	0	0	8	7
71-11	5	S 5.00000	42	83	Y	6	8	0	0	0	0	6	8
71-11	5	S 5.00000	42	84	Y	8	8	0	0	0	1	9	8
71-11	5	S 5.00000	43	85	Y	8	7	0	0	0	0	8	7
71-11	5	S 5.00000	43	86	Y	4	7	2	0	0	1	6	7
71-11	5	S 5.00000	44	87	Y	8	8	0	0	0	0	8	9
71-11	5	S 5.00000	44	88	Y	7	6	0	0	0	0	7	7
71-11	5	S 5.00000	45	89	Y	4	12	0	0	0	0	5	14
71-11	5	S 5.00000	45	90	Y	7	6	0	0	0	0	10	6
71-11	5	S 5.00000	46	91	Y	7	7	0	1	0	1	7	7
71-11	5	S 5.00000	46	92	Y	4	8	0	0	0	0	4	8
71-11	5	S 5.00000	47	93	Y	8	6	1	0	0	0	10	6
71-11	5	S 5.00000	47	94	Y	8	6	0	0	0	0	8	6
71-11	5	S 5.00000	48	95	Y	12	3	0	0	0	0	13	3
71-11	5	S 5.00000	48	96	Y	9	5	1	0	0	0	9	5
71-11	5	S 5.00000	49	97	Y	7	7	1	0	0	1	7	7
71-11	5	S 5.00000	49	98	Y	4	10	0	0	0	0	4	10
71-11	5	S 5.00000	50	99	Y	7	7	1	0	0	0	8	7
71-11	5	S 5.00000	50	100	Y	9	4	0	0	1	0	10	7

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SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	H	L	R	L	H
TEM	5	S	.00020	11	21	Y	6	6	0	1	0	0	6	6
TFM	5	S	.00020	11	22	Y	7	3	0	0	1	1	8	3
TFM	5	S	.00020	12	23	Y	6	5	0	0	0	0	6	5
TEM	5	S	.00020	12	24	Y	5	8	1	0	1	2	6	8
TEM	5	S	.00020	13	25	Y	6	6	1	0	0	0	6	10
TEM	5	S	.00020	13	26	Y	3	3	3	2	0	0	6	3
TEM	5	S	.00020	14	27	Y	3	8	1	2	0	0	4	8
TEM	5	S	.00020	14	28	Y	3	7	2	1	0	0	6	7
TEM	5	S	.00020	15	29	Y	5	8	2	1	0	0	5	8
TEM	5	S	.00020	15	30	Y	5	10	0	0	0	0	5	10
TEM	5	S	.00020	16	31	Y	9	4	3	1	0	0	9	4
TEM	5	S	.00020	16	32	Y	9	5	0	0	0	0	9	5
TEM	5	S	.00020	17	33	Y	4	6	4	1	0	0	5	9
TFM	5	S	.00020	17	34	Y	4	9	2	3	0	0	4	9
TEM	5	S	.00020	18	35	Y	3	7	0	6	0	0	3	7
TEM	5	S	.00020	18	36	Y	9	5	2	0	1	2	10	5
TEM	5	S	.00020	19	37	Y	8	3	0	0	0	0	8	3
TEM	5	S	.00020	19	38	Y	5	5	2	2	0	0	5	5
TEM	5	S	.00020	20	39	Y	5	7	1	2	0	0	5	8
TFM	5	S	.00020	20	40	Y	7	2	4	0	1	1	8	3
CONTROL	5	M	0.00000	1	1	Y	9	6	0	0	0	0	9	6
CONTROL	5	M	0.00000	1	2	Y	2	2	2	0	0	0	8	3
CONTROL	5	M	0.00000	2	3	YY	8	7	0	0	0	0	8	7
CONTROL	5	M	0.00000	2	4	YY	5	9	0	0	1	0	6	9
CONTROL	5	M	0.00000	3	5	YY	7	5	0	0	0	0	8	5
CONTROL	5	M	0.00000	3	6	YY	7	4	0	0	0	0	8	4
CONTROL	5	M	0.00000	4	7	YY	10	9	0	0	0	0	10	7
CONTROL	5	M	0.00000	4	8	YY	5	5	0	0	1	0	10	6
CONTROL	5	M	0.00000	5	9	YY	7	6	1	0	0	0	8	6
CONTROL	5	M	0.00000	5	10	YY	5	11	0	0	0	0	5	11
CONTROL	5	M	0.00000	6	11	YY	2	0	0	0	0	0	6	6
CONTROL	5	M	0.00000	6	12	YY	4	0	0	1	0	0	4	9
CONTROL	5	M	0.00000	7	13	YY	10	4	4	2	0	0	11	8
CONTROL	5	M	0.00000	7	14	YY	0	2	0	0	0	0	8	6
CONTROL	5	M	0.00000	8	15	NN	0	0	0	0	0	0	0	0
CONTROL	5	M	0.00000	8	16	NN	0	0	0	0	0	0	0	0
CONTROL	5	M	0.00000	9	17	YY	6	7	0	0	0	0	6	7
CONTROL	5	M	0.00000	9	18	YY	9	6	0	0	2	0	9	6
CONTROL	5	M	0.00000	10	19	YY	7	7	0	0	0	0	7	7
CONTROL	5	M	0.00000	10	20	YY	6	6	1	0	0	0	7	7

DOMINANT LETHAL STUDY OF COMPOUND 71-11

SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	H	L	R	L	H	L	K
71-11	5	M	.20000	11	21	Y	4	8	0	0	0	0	6	12
71-11	5	M	.20000	11	22	Y	4	9	1	0	0	0	4	11
71-11	5	M	.20000	12	23	Y	3	10	0	0	0	1	3	10
71-11	5	M	.20000	12	24	Y	7	6	0	0	0	0	8	7
71-11	5	M	.20000	13	25	Y	5	8	0	0	0	0	5	8
71-11	5	M	.20000	13	26	Y	5	8	0	0	0	0	7	9
71-11	5	M	.20000	14	27	Y	7	6	0	0	2	4	7	6
71-11	5	M	.20000	14	28	Y	7	8	0	1	0	0	7	11
71-11	5	M	.20000	15	29	Y	9	7	0	0	0	0	12	7
71-11	5	M	.20000	15	30	Y	7	7	0	0	0	0	7	9
71-11	5	M	.20000	16	31	Y	4	6	1	0	0	0	5	6
71-11	5	M	.20000	16	32	Y	6	6	0	0	0	0	8	6
71-11	5	M	.20000	17	33	Y	10	6	0	0	0	0	10	6
71-11	5	M	.20000	17	34	Y	10	4	0	0	0	0	10	6
71-11	5	M	.20000	18	35	N	0	0	0	0	0	0	0	0
71-11	5	M	.20000	18	36	Y	5	9	0	0	1	2	5	9
71-11	5	M	.20000	19	37	Y	4	7	0	0	0	0	4	7
71-11	5	M	.20000	19	38	Y	9	4	0	0	0	0	9	5
71-11	5	M	.20000	20	39	Y	3	7	0	1	0	0	4	9
71-11	5	M	.20000	20	40	N	0	0	0	0	0	0	0	0
71-11	5	M	1.00000	21	41	Y	7	6	0	0	0	0	7	6
71-11	5	M	1.00000	21	42	Y	4	5	0	1	0	0	8	7
71-11	5	M	1.00000	22	43	Y	5	7	0	0	1	0	6	7
71-11	5	M	1.00000	22	44	Y	6	7	0	0	0	0	7	9
71-11	5	M	1.00000	23	45	Y	6	4	0	0	0	0	6	4
71-11	5	M	1.00000	23	46	Y	5	5	0	0	0	0	5	5
71-11	5	M	1.00000	24	47	Y	8	8	1	0	0	0	11	15
71-11	5	M	1.00000	24	48	Y	4	7	0	0	2	2	4	8
71-11	5	M	1.00000	25	49	Y	3	4	0	0	1	0	9	9
71-11	5	M	1.00000	25	50	Y	8	6	0	0	0	0	8	6
71-11	5	M	1.00000	26	51	Y	7	7	0	0	1	1	7	7
71-11	5	M	1.00000	26	52	N	0	0	0	0	0	0	0	0
71-11	5	M	1.00000	27	53	Y	9	4	0	0	0	0	9	4
71-11	5	M	1.00000	27	54	Y	7	7	1	0	0	0	8	8
71-11	5	M	1.00000	28	55	Y	6	9	0	0	1	0	6	9
71-11	5	M	1.00000	28	56	N	0	0	0	0	0	0	0	0
71-11	5	M	1.00000	29	57	N	0	0	0	0	0	0	0	0
71-11	5	M	1.00000	29	58	Y	6	6	0	0	0	0	6	6
71-11	5	M	1.00000	30	59	N	0	0	0	0	0	0	0	0
71-11	5	M	1.00000	30	60	Y	7	5	0	0	0	0	8	5

DOMINANT LETHAL STUDY OF COMPOUND 71-11

SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		COMPOUNDS LUTEA		
							L	R	L	R	L	R	
71-11	5	M 5.00000	31	61	Y	5	7	0	0	0	0	6	7
71-11	5	M 5.00000	31	62	Y	9	3	2	0	0	0	10	4
71-11	5	M 5.00000	32	63	Y	2	9	0	0	0	0	2	9
71-11	5	M 5.00000	32	64	YY	6	6	0	1	0	0	6	6
71-11	5	M 5.00000	33	65	Y	6	7	1	1	0	0	7	10
71-11	5	M 5.00000	33	66	YY	6	6	0	0	0	0	6	9
71-11	5	M 5.00000	34	67	Y	4	9	0	1	0	0	4	9
71-11	5	M 5.00000	34	68	YY	6	6	0	0	0	0	6	6
71-11	5	M 5.00000	35	69	YY	7	7	0	0	0	0	8	8
71-11	5	M 5.00000	35	70	YY	5	9	0	0	0	0	5	10
71-11	5	M 5.00000	36	71	YY	6	6	0	0	0	0	6	6
71-11	5	M 5.00000	36	72	YY	2	11	1	3	0	0	2	13
71-11	5	M 5.00000	37	73	YY	5	5	0	0	0	0	6	8
71-11	5	M 5.00000	37	74	YY	5	3	0	0	0	0	6	3
71-11	5	M 5.00000	38	75	YY	5	9	0	0	0	0	5	10
71-11	5	M 5.00000	38	76	YY	3	7	0	0	0	0	3	7
71-11	5	M 5.00000	39	77	YY	6	7	0	0	1	2	8	7
71-11	5	M 5.00000	39	78	YY	7	6	2	0	0	0	7	6
71-11	5	M 5.00000	40	79	YY	3	4	0	0	0	0	3	7
71-11	5	M 5.00000	40	80	Y	7	6	0	0	1	0	8	6

DOMINANT LETHAL STUDY OF COMPOUND 71-11

SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		COMPOUND LUTEA		
							L	R	L	R	L	R	L
CONTROL	6	S 0.00000	1	1	Y	4	5	0	0	0	0	6	5
CONTROL	6	S 0.00000	1	2	YY	5	3	0	1	0	0	5	6
CONTROL	6	S 0.00000	2	3	YY	6	7	1	0	0	0	6	8
CONTROL	6	S 0.00000	2	4	YY	6	2	1	1	1	0	8	4
CONTROL	6	S 0.00000	3	5	YY	3	7	0	0	0	0	4	8
CONTROL	6	S 0.00000	3	6	YY	6	5	0	0	0	0	6	5
CONTROL	6	S 0.00000	4	7	YY	6	6	1	1	0	0	6	6
CONTROL	6	S 0.00000	4	8	YY	5	9	0	0	0	0	6	9
CONTROL	6	S 0.00000	5	9	YY	6	5	1	0	0	0	6	8
CONTROL	6	S 0.00000	5	10	YY	7	5	0	0	0	0	7	5
CONTROL	6	S 0.00000	6	11	YY	6	4	1	0	0	0	6	4
CONTROL	6	S 0.00000	6	12	YY	7	5	0	0	0	0	7	6
CONTROL	6	S 0.00000	7	13	YY	4	6	0	0	0	0	4	6
CONTROL	6	S 0.00000	7	14	YY	5	8	0	1	0	0	5	9
CONTROL	6	S 0.00000	8	15	YY	8	6	0	0	0	0	8	6
CONTROL	6	S 0.00000	8	16	YY	4	7	0	1	0	0	5	7
CONTROL	6	S 0.00000	9	17	YY	3	8	0	0	0	0	3	8
CONTROL	6	S 0.00000	9	18	YY	8	6	0	0	0	0	8	6
CONTROL	6	S 0.00000	10	19	YY	5	8	1	0	1	0	6	8
CONTROL	6	S 0.00000	10	20	Y	10	4	0	1	0	0	10	4
71-11	6	S .20000	21	41	Y	7	8	0	1	0	0	7	8
71-11	6	S .20000	21	42	YY	5	12	0	0	0	1	7	12
71-11	6	S .20000	22	43	YY	7	6	0	0	0	1	7	6
71-11	6	S .20000	22	44	YY	5	5	2	0	0	0	5	8
71-11	6	S .20000	23	45	YY	4	7	0	0	0	0	4	7
71-11	6	S .20000	23	46	YY	5	4	0	0	0	1	9	5
71-11	6	S .20000	24	47	YY	8	7	1	0	0	1	8	8
71-11	6	S .20000	24	48	YY	2	1	0	0	0	1	8	7
71-11	6	S .20000	25	49	YY	9	6	0	0	0	0	9	6
71-11	6	S .20000	25	50	YY	8	4	0	0	0	0	9	6
71-11	6	S .20000	26	51	YY	5	7	0	1	0	0	5	8
71-11	6	S .20000	26	52	YY	8	7	0	0	0	0	8	7
71-11	6	S .20000	27	53	YY	4	8	0	0	0	0	4	9
71-11	6	S .20000	27	54	YY	4	9	0	0	0	1	4	9
71-11	6	S .20000	28	55	YY	6	6	0	0	0	1	6	7
71-11	6	S .20000	28	56	YY	6	7	0	0	0	1	6	7
71-11	6	S .20000	29	57	YY	7	5	0	0	0	0	7	6
71-11	6	S .20000	29	58	YY	6	6	0	0	0	0	7	7
71-11	6	S .20000	30	59	YY	4	10	0	0	1	1	4	10
71-11	6	S .20000	30	60	Y	6	3	0	1	1	0	9	3

DOMINANT LETHAL STUDY OF COMPOUND 71-11

SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
						L	R	L	R	L	R	L	H
71-11	6	S 1.00000	31	61	Y	7	7	0	0	0	0	7	7
71-11	6	S 1.00000	31	62	YY	8	5	0	0	0	0	9	5
71-11	6	S 1.00000	32	63	YY	7	4	0	0	0	0	7	5
71-11	6	S 1.00000	32	64	YY	10	3	2	0	0	0	10	3
71-11	6	S 1.00000	33	65	YY	8	5	0	0	0	0	8	5
71-11	6	S 1.00000	33	66	YY	4	9	0	0	0	0	4	9
71-11	6	S 1.00000	34	67	YY	6	10	0	0	0	0	6	10
71-11	6	S 1.00000	34	68	YY	8	3	0	0	0	0	8	3
71-11	6	S 1.00000	35	69	YY	6	6	0	0	2	1	6	6
71-11	6	S 1.00000	35	70	NY	0	0	0	0	0	0	0	0
71-11	6	S 1.00000	36	71	YY	6	7	0	0	0	0	6	7
71-11	6	S 1.00000	36	72	YY	9	2	1	0	0	0	9	2
71-11	6	S 1.00000	37	73	YY	0	6	0	0	0	0	4	6
71-11	6	S 1.00000	37	74	YY	2	9	0	0	0	0	2	9
71-11	6	S 1.00000	38	75	YY	6	4	0	0	1	0	6	4
71-11	6	S 1.00000	38	76	NY	0	0	0	0	0	0	0	0
71-11	6	S 1.00000	39	77	YY	5	8	1	1	0	0	5	8
71-11	6	S 1.00000	39	78	NY	0	0	0	0	0	0	0	0
71-11	6	S 1.00000	40	79	YY	5	5	0	1	1	3	5	5
71-11	6	S 1.00000	40	80	Y	6	7	1	1	0	0	7	7
71-11	6	S 5.00000	41	81	YY	5	7	0	1	1	0	6	7
71-11	6	S 5.00000	41	82	YY	6	7	0	0	0	0	6	7
71-11	6	S 5.00000	42	83	YY	1	0	1	0	0	0	7	4
71-11	6	S 5.00000	42	84	YY	4	8	0	1	0	0	4	8
71-11	6	S 5.00000	43	85	YY	5	7	0	0	2	5	5	7
71-11	6	S 5.00000	43	86	YY	3	8	1	4	0	0	3	8
71-11	6	S 5.00000	44	87	YY	7	5	0	0	0	0	7	5
71-11	6	S 5.00000	44	88	YY	7	4	1	0	0	0	8	4
71-11	6	S 5.00000	45	89	YY	5	8	0	1	1	0	5	8
71-11	6	S 5.00000	45	90	YY	6	3	1	0	0	0	7	4
71-11	6	S 5.00000	46	91	YY	9	8	0	0	1	0	9	8
71-11	6	S 5.00000	46	92	YY	4	8	1	0	0	0	4	10
71-11	6	S 5.00000	47	93	YY	5	8	0	2	0	0	5	10
71-11	6	S 5.00000	47	94	YY	6	8	0	0	0	0	6	8
71-11	6	S 5.00000	48	95	YY	5	8	0	0	0	0	5	8
71-11	6	S 5.00000	48	96	YY	8	7	0	0	0	0	8	8
71-11	6	S 5.00000	49	97	YY	5	7	0	0	0	0	7	7
71-11	6	S 5.00000	49	98	NY	0	0	0	0	0	0	0	0
71-11	6	S 5.00000	50	99	Y	0	0	1	0	0	0	3	0

DOMINANT LETHAL STUDY OF COMPOUND 71-11

SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS			LATE DEATHS			COMPOUND LUTEA	
								L	R	L	H	L	R	L	R
TEM	6	S	.00020	11	21	Y	4	8	0	0	0	0	0	4	8
TEM	6	S	.00020	11	22	Y	8	6	0	0	0	0	0	8	6
TEM	6	S	.00020	12	23	Y	6	6	1	1	0	0	0	7	6
TEM	6	S	.00020	12	24	Y	3	8	0	0	1	0	0	3	8
TEM	6	S	.00020	13	25	Y	6	7	0	0	0	0	0	5	8
TEM	6	S	.00020	13	26	Y	5	8	0	0	0	0	0	8	7
TEM	6	S	.00020	14	27	Y	8	6	0	0	0	0	0	8	7
TEM	6	S	.00020	14	28	Y	7	7	0	0	0	0	0	5	6
TEM	6	S	.00020	15	29	Y	5	6	0	0	0	0	0	8	7
TEM	6	S	.00020	15	30	Y	8	7	0	0	0	0	0	3	4
TEM	6	S	.00020	16	31	Y	3	5	0	0	0	0	0	6	6
TEM	6	S	.00020	16	32	Y	6	6	0	0	1	0	0	6	7
TEM	6	S	.00020	17	33	Y	6	7	1	1	0	0	0	8	8
TEM	6	S	.00020	17	34	Y	7	5	0	0	0	0	0	4	10
TEM	6	S	.00020	18	35	Y	4	10	0	1	0	0	0	6	6
TEM	6	S	.00020	18	36	Y	6	6	0	0	0	0	0	8	4
TEM	6	S	.00020	19	37	Y	8	4	0	0	0	0	0	6	8
TEM	6	S	.00020	19	38	Y	6	8	0	0	0	0	0	3	11
TEM	6	S	.00020	20	39	Y	3	9	0	0	0	0	0	7	9
TEM	6	S	.00020	20	40	Y	7	8	0	0	0	0	0	7	9
CONTROL	6	M	0.00000	1	1	Y	4	8	0	0	0	0	0	5	8
CONTROL	6	M	0.00000	1	2	Y	7	5	0	0	1	0	0	7	5
CONTROL	6	M	0.00000	2	3	YY	10	2	0	0	0	0	0	10	2
CONTROL	6	M	0.00000	2	4	YY	7	6	0	0	0	0	0	6	6
CONTROL	6	M	0.00000	3	5	YY	5	6	0	0	1	1	0	5	7
CONTROL	6	M	0.00000	3	6	Y	7	7	0	0	1	1	0	10	4
CONTROL	6	M	0.00000	4	7	YY	10	4	0	0	0	0	0	10	5
CONTROL	6	M	0.00000	4	8	YY	6	5	0	0	0	0	0	10	5
CONTROL	6	M	0.00000	5	9	YY	10	5	1	0	0	0	0	7	9
CONTROL	6	M	0.00000	5	10	YY	7	7	0	0	0	0	0	6	4
CONTROL	6	M	0.00000	6	11	YY	6	4	0	0	0	0	0	6	5
CONTROL	6	M	0.00000	6	12	YY	6	5	0	0	0	0	0	6	6
CONTROL	6	M	0.00000	7	13	YY	7	4	0	0	0	0	0	7	6
CONTROL	6	M	0.00000	7	14	YY	9	4	2	1	0	0	0	9	4
CONTROL	6	M	0.00000	8	15	YY	5	8	0	0	0	0	0	5	8
CONTROL	6	M	0.00000	8	16	YY	8	6	0	0	0	0	0	11	6
CONTROL	6	M	0.00000	9	17	YY	6	5	0	0	1	0	0	7	7
CONTROL	6	M	0.00000	9	18	YY	7	7	0	0	0	0	0	4	11
CONTROL	6	M	0.00000	10	19	YY	0	7	0	0	0	0	0	7	7
CONTROL	6	M	0.00000	10	20	Y	0	7	0	0	0	0	0	4	11

DOMINANT LETHAL STUDY OF COMPOUND 71-11

SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA		
								L	H	L	H	L	R	
71-11	6	M	.20000	11	21	Y	6	6	0	0	0	0	6	6
71-11	6	M	.20000	11	22	YY	9	2	0	0	0	0	9	4
71-11	6	M	.20000	12	23	YY	6	5	0	0	0	0	6	6
71-11	6	M	.20000	12	24	YY	1	0	0	0	0	0	9	5
71-11	6	M	.20000	13	25	YY	7	6	1	0	0	0	7	6
71-11	6	M	.20000	13	26	YY	5	7	0	0	0	0	6	7
71-11	6	M	.20000	14	27	YY	6	6	0	0	1	0	7	6
71-11	6	M	.20000	14	28	YY	3	10	0	0	0	2	3	11
71-11	6	M	.20000	15	29	YY	6	7	0	0	0	0	6	7
71-11	6	M	.20000	15	30	Y	6	6	0	0	0	0	6	7
71-11	6	M	.20000	16	31	YY	6	6	0	0	0	0	6	8
71-11	6	M	.20000	16	32	YY	5	7	0	0	0	0	5	7
71-11	6	M	.20000	17	33	YY	5	6	1	0	0	0	5	6
71-11	6	M	.20000	17	34	YY	6	7	0	0	0	1	6	5
71-11	6	M	.20000	18	35	YY	6	5	1	0	2	2	6	4
71-11	6	M	.20000	18	36	YY	10	4	1	0	0	0	10	4
71-11	6	M	.20000	19	37	YY	3	11	0	0	0	0	3	12
71-11	6	M	.20000	19	38	YY	4	8	0	0	1	0	4	8
71-11	6	M	.20000	20	39	YY	5	5	0	0	0	0	6	6
71-11	6	M	.20000	20	40	Y	7	4	0	0	1	0	7	4
71-11	6	M	1.00000	21	41	Y	6	5	0	0	0	0	6	5
71-11	6	M	1.00000	21	42	YY	2	10	0	0	0	0	2	11
71-11	6	M	1.00000	22	43	YY	5	6	0	0	0	1	6	6
71-11	6	M	1.00000	22	44	YY	7	3	0	0	0	0	8	5
71-11	6	M	1.00000	23	45	YY	8	6	0	0	0	0	8	7
71-11	6	M	1.00000	23	46	YY	6	9	0	0	0	0	6	9
71-11	6	M	1.00000	24	47	YY	9	4	0	0	0	0	9	4
71-11	6	M	1.00000	24	48	YY	7	5	0	0	2	2	8	5
71-11	6	M	1.00000	25	49	YY	7	5	0	0	0	0	8	5
71-11	6	M	1.00000	25	50	YY	5	8	0	0	0	0	5	8
71-11	6	M	1.00000	26	51	YY	6	6	1	1	1	1	6	6
71-11	6	M	1.00000	26	52	YY	5	9	1	1	1	3	5	10
71-11	6	M	1.00000	27	53	YY	2	4	0	0	0	0	8	4
71-11	6	M	1.00000	27	54	YY	5	7	0	1	0	0	8	6
71-11	6	M	1.00000	28	55	YY	8	6	0	0	0	0	8	6
71-11	6	M	1.00000	28	56	YY	6	9	0	0	0	0	6	9
71-11	6	M	1.00000	29	57	YY	8	7	2	0	0	0	9	7
71-11	6	M	1.00000	29	58	YY	4	7	0	0	0	0	4	7
71-11	6	M	1.00000	30	59	YY	5	8	0	1	0	1	5	8
71-11	6	M	1.00000	30	60	Y	4	8	0	0	0	0	4	8

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
						L	R	L	R	L	R	L	R
71-11	6	M 5.00000	31	61	Y	5	8	1	4	0	0	5	8
71-11	6	M 5.00000	31	62	Y	3	8	1	0	0	1	3	8
71-11	6	M 5.00000	32	63	Y	4	11	0	0	1	0	4	11
71-11	6	M 5.00000	32	64	Y	8	6	0	0	0	0	8	6
71-11	6	M 5.00000	33	65	Y	9	4	1	0	0	0	10	6
71-11	6	M 5.00000	33	66	Y	7	9	0	0	2	2	7	10
71-11	6	M 5.00000	34	67	Y	4	8	0	0	0	0	5	10
71-11	6	M 5.00000	34	68	Y	11	4	1	0	0	0	11	4
71-11	6	M 5.00000	35	69	Y	6	4	0	0	0	0	7	4
71-11	6	M 5.00000	35	70	Y	9	4	2	0	0	0	9	4
71-11	6	M 5.00000	36	71	Y	7	8	0	0	0	0	8	8
71-11	6	M 5.00000	36	72	Y	4	11	0	1	0	0	4	11
71-11	6	M 5.00000	37	73	Y	10	3	0	0	0	1	10	3
71-11	6	M 5.00000	37	74	Y	7	5	0	0	0	0	7	6
71-11	6	M 5.00000	38	75	N	0	0	0	0	0	0	0	0
71-11	6	M 5.00000	38	76	Y	2	13	1	0	0	2	2	13
71-11	6	M 5.00000	39	77	Y	4	6	0	0	1	0	4	6
71-11	6	M 5.00000	39	78	Y	5	6	0	0	0	0	6	6
71-11	6	M 5.00000	40	79	Y	6	7	0	0	0	0	6	7
71-11	6	M 5.00000	40	80	Y	7	4	0	0	0	0	7	4

DOMINANT LETHAL STUDY OF COMPOUND 71-1

SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA		
								L	R	L	R	L	R	
CONTROL	7	S	0.00000	1	1	Y	7	5	0	0	0	0	7	8
CONTROL	7	S	0.00000	1	2	YY	0	1	0	0	0	0	7	2
CONTROL	7	S	0.00000	2	3	YY	6	8	0	0	0	0	6	8
CONTROL	7	S	0.00000	2	4	YY	6	6	0	0	0	0	7	6
CONTROL	7	S	0.00000	3	5	YY	0	3	0	0	0	0	4	3
CONTROL	7	S	0.00000	3	6	YY	5	7	0	0	0	0	5	7
CONTROL	7	S	0.00000	4	7	YY	6	9	0	0	0	0	6	9
CONTROL	7	S	0.00000	4	8	YY	11	5	1	0	0	0	11	10
CONTROL	7	S	0.00000	5	9	YY	8	5	0	0	0	0	7	7
CONTROL	7	S	0.00000	5	10	YY	5	8	0	0	0	0	5	8
CONTROL	7	S	0.00000	6	11	YY	6	5	0	0	0	0	7	5
CONTROL	7	S	0.00000	6	12	YY	8	9	0	0	0	0	8	9
CONTROL	7	S	0.00000	7	13	YY	6	5	0	0	0	0	6	6
CONTROL	7	S	0.00000	7	14	YY	3	8	0	0	0	0	3	3
CONTROL	7	S	0.00000	8	15	YY	6	5	0	0	0	0	6	6
CONTROL	7	S	0.00000	8	16	YY	6	6	1	0	1	0	7	7
CONTROL	7	S	0.00000	9	17	YY	0	1	0	0	0	0	6	6
CONTROL	7	S	0.00000	9	18	YY	9	5	0	0	0	0	9	5
CONTROL	7	S	0.00000	10	19	YY	5	8	0	0	0	0	8	8
CONTROL	7	S	0.00000	10	20	Y	8	6	0	0	0	0	6	6
71-11	7	S	.20000	21	41	Y	4	9	0	1	0	0	4	9
71-11	7	S	.20000	21	42	YY	6	8	0	0	0	0	6	8
71-11	7	S	.20000	22	43	YY	6	8	0	0	0	0	6	8
71-11	7	S	.20000	22	44	YY	7	8	0	0	0	0	7	10
71-11	7	S	.20000	23	45	YY	5	9	0	0	0	0	6	6
71-11	7	S	.20000	23	46	YY	4	9	0	0	0	0	4	9
71-11	7	S	.20000	24	47	YY	8	5	0	0	0	0	8	5
71-11	7	S	.20000	24	48	YY	2	8	0	0	0	0	10	11
71-11	7	S	.20000	25	49	YY	5	7	0	0	0	0	7	6
71-11	7	S	.20000	25	50	YY	5	6	0	0	0	0	6	5
71-11	7	S	.20000	26	51	YY	6	5	0	0	0	0	6	6
71-11	7	S	.20000	26	52	YY	7	5	0	0	0	0	8	6
71-11	7	S	.20000	27	53	YY	7	4	0	0	0	0	7	7
71-11	7	S	.20000	27	54	YY	5	7	0	0	0	0	5	3
71-11	7	S	.20000	28	55	YY	6	3	0	0	0	0	9	5
71-11	7	S	.20000	28	56	YY	8	5	0	0	1	0	4	4
71-11	7	S	.20000	29	57	YY	6	4	0	0	0	0	7	8
71-11	7	S	.20000	29	58	YY	7	7	0	0	0	0	7	7
71-11	7	S	.20000	30	59	YY	5	7	0	0	0	0	0	0
71-11	7	S	.20000	30	60	YY	4	11	0	0	0	0	0	0

DOMINANT LETHAL STUDY OF COMPOUND 71-11

SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA		
							L	R	L	R	L	R	
71-11	7	S 1.00000	31	61	Y	5	7	0	0	1	0	5	7
71-11	7	S 1.00000	31	62	YY	5	7	0	0	0	0	7	7
71-11	7	S 1.00000	32	63	YY	8	4	0	0	0	0	8	4
71-11	7	S 1.00000	32	64	YY	5	7	0	0	1	0	5	7
71-11	7	S 1.00000	33	65	Y	6	6	0	0	0	0	7	6
71-11	7	S 1.00000	33	66	YY	5	6	0	0	0	0	5	6
71-11	7	S 1.00000	34	67	YY	5	8	0	0	0	0	5	8
71-11	7	S 1.00000	34	68	YY	6	5	0	0	0	1	6	6
71-11	7	S 1.00000	35	69	YY	9	4	0	0	0	0	9	4
71-11	7	S 1.00000	35	70	Y	5	8	0	0	0	0	5	8
71-11	7	S 1.00000	36	71	YY	6	10	0	0	0	0	6	10
71-11	7	S 1.00000	36	72	YY	3	6	0	0	0	0	3	10
71-11	7	S 1.00000	37	73	YY	8	6	0	0	0	0	8	6
71-11	7	S 1.00000	37	74	YY	0	2	0	0	0	1	4	6
71-11	7	S 1.00000	38	75	YY	5	3	2	0	0	0	6	5
71-11	7	S 1.00000	38	76	YY	7	5	0	0	0	0	7	5
71-11	7	S 1.00000	39	77	YY	3	0	0	0	0	0	6	5
71-11	7	S 1.00000	39	78	YY	9	3	0	0	0	0	12	4
71-11	7	S 1.00000	40	79	YY	8	7	0	1	0	0	9	7
71-11	7	S 1.00000	40	80	Y	8	7	0	0	0	0	8	7
71-11	7	S 5.00000	41	81	Y	6	6	0	1	0	0	6	6
71-11	7	S 5.00000	41	82	YY	7	8	0	2	0	0	7	8
71-11	7	S 5.00000	42	83	YY	5	7	0	1	0	0	5	7
71-11	7	S 5.00000	42	84	YY	9	4	0	0	0	0	9	4
71-11	7	S 5.00000	43	85	YY	7	5	0	1	0	0	7	5
71-11	7	S 5.00000	43	86	YY	7	5	0	0	0	0	7	5
71-11	7	S 5.00000	44	87	YY	5	7	0	0	0	0	5	7
71-11	7	S 5.00000	44	88	YY	7	6	0	0	0	0	7	6
71-11	7	S 5.00000	45	89	YY	4	10	0	0	0	0	4	12
71-11	7	S 5.00000	45	90	YY	5	9	0	0	0	0	5	9
71-11	7	S 5.00000	46	91	YY	5	6	0	0	0	0	5	6
71-11	7	S 5.00000	46	92	YY	4	8	0	0	0	0	4	8
71-11	7	S 5.00000	47	93	YY	4	8	0	0	0	0	4	8
71-11	7	S 5.00000	47	94	Y	9	3	1	0	0	0	9	3
71-11	7	S 5.00000	48	95	YY	3	7	0	0	0	0	3	8
71-11	7	S 5.00000	48	96	YY	7	7	0	0	0	0	7	7
71-11	7	S 5.00000	49	97	YY	2	12	0	0	0	0	2	12
71-11	7	S 5.00000	49	98	YY	5	9	0	0	0	0	6	9
71-11	7	S 5.00000	50	99	N	0	0	0	0	0	0	0	0
71-11	7	S 5.00000	50	100	Y	9	3	1	0	0	0	10	4

DOMINANT LETHAL STUDY OF COMPOUND 71-11

SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	R	L	R	L	H
TEM	7	S	.00020	11	21	Y	10	5	0	1	0	0	10	5
TEM	7	S	.00020	11	22	Y	9	2	0	0	0	1	9	2
TEM	7	S	.00020	12	23	Y	4	9	0	1	0	0	4	9
TEM	7	S	.00020	12	24	Y	6	8	0	1	0	0	6	8
TEM	7	S	.00020	13	25	Y	6	5	0	0	0	0	6	7
TEM	7	S	.00020	13	26	Y	11	1	0	0	0	0	11	2
TEM	7	S	.00020	14	27	Y	7	9	0	0	0	0	8	9
TEM	7	S	.00020	14	28	Y	6	5	0	1	0	0	8	5
TEM	7	S	.00020	15	29	Y	6	8	0	0	0	0	6	8
TEM	7	S	.00020	15	30	Y	5	7	0	1	0	0	5	7
TEM	7	S	.00020	16	31	Y	5	8	0	0	0	0	5	8
TEM	7	S	.00020	16	32	Y	8	5	0	0	0	0	8	5
TEM	7	S	.00020	17	33	Y	9	7	0	0	1	0	9	7
TEM	7	S	.00020	17	34	Y	8	6	0	0	3	0	9	6
TEM	7	S	.00020	18	35	Y	8	4	0	0	0	0	9	4
TEM	7	S	.00020	18	36	Y	4	7	0	1	1	1	4	9
TEM	7	S	.00020	19	37	Y	7	7	1	0	0	0	7	7
TEM	7	S	.00020	19	38	Y	1	11	0	0	0	0	1	12
TEM	7	S	.00020	20	39	Y	5	8	0	0	0	0	7	8
TEM	7	S	.00020	20	40	Y	7	7	0	0	0	0	7	7
CONTROL	7	M	0.00000	1	1	Y	6	7	0	0	0	0	6	8
CONTROL	7	M	0.00000	1	2	Y	0	9	0	0	0	0	2	9
CONTROL	7	M	0.00000	2	3	Y	9	8	0	0	0	0	9	8
CONTROL	7	M	0.00000	2	4	Y	5	5	2	2	0	0	8	5
CONTROL	7	M	0.00000	3	5	Y	5	9	1	0	0	1	5	10
CONTROL	7	M	0.00000	3	6	Y	2	0	2	0	0	0	4	6
CONTROL	7	M	0.00000	4	7	Y	4	6	0	0	0	0	5	6
CONTROL	7	M	0.00000	4	8	Y	4	8	1	2	0	0	5	9
CONTROL	7	M	0.00000	5	9	Y	7	5	0	0	0	0	7	5
CONTROL	7	M	0.00000	5	10	Y	7	5	1	0	0	0	8	5
CONTROL	7	M	0.00000	6	11	Y	7	8	0	0	0	0	7	9
CONTROL	7	M	0.00000	6	12	Y	5	7	0	0	0	0	5	7
CONTROL	7	M	0.00000	7	13	Y	7	4	0	2	1	0	7	4
CONTROL	7	M	0.00000	7	14	Y	7	4	2	1	0	0	7	4
CONTROL	7	M	0.00000	8	15	Y	8	5	0	0	0	0	8	6
CONTROL	7	M	0.00000	8	16	Y	6	4	1	1	0	0	6	4
CONTROL	7	M	0.00000	9	17	Y	7	6	0	1	0	0	7	6
CONTROL	7	M	0.00000	9	18	Y	6	9	0	1	0	0	6	10
CONTROL	7	M	0.00000	10	19	Y	5	6	0	0	0	0	6	6
CONTROL	7	M	0.00000	10	20	Y	9	1	2	0	0	0	5	10

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SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORAL LUTEA	
								L	R	L	R	L	H
71-11	7	M	.20000	11	21	Y	7	7	0	0	0	0	7
71-11	7	M	.20000	11	22	YY	5	7	0	0	0	0	5
71-11	7	M	.20000	12	23	YY	4	9	0	0	0	0	4
71-11	7	M	.20000	12	24	YY	6	6	1	1	0	0	6
71-11	7	M	.20000	13	25	YY	8	4	0	0	0	0	8
71-11	7	M	.20000	13	26	YY	3	2	1	0	0	0	9
71-11	7	M	.20000	14	27	YY	8	5	0	0	0	0	8
71-11	7	M	.20000	15	28	YY	2	10	0	0	0	0	5
71-11	7	M	.20000	15	29	YY	6	6	0	0	1	0	7
71-11	7	M	.20000	15	30	YY	6	6	0	0	0	0	6
71-11	7	M	.20000	16	31	YY	6	8	1	0	0	0	6
71-11	7	M	.20000	16	32	YY	5	9	0	1	0	0	5
71-11	7	M	.20000	17	33	YY	3	5	0	0	0	0	3
71-11	7	M	.20000	17	34	YY	4	7	0	0	0	0	5
71-11	7	M	.20000	18	35	YY	7	7	2	0	0	0	9
71-11	7	M	.20000	18	36	YY	5	8	3	4	0	0	8
71-11	7	M	.20000	19	37	YY	6	7	0	0	0	0	6
71-11	7	M	.20000	19	38	YY	8	5	0	0	0	0	7
71-11	7	M	.20000	20	39	YY	5	10	0	0	0	0	6
71-11	7	M	.20000	20	40	YY	6	5	0	0	0	0	10
71-11	7	M	1.00000	21	41	YY	6	6	1	0	0	0	6
71-11	7	M	1.00000	21	42	YY	3	7	0	0	0	0	7
71-11	7	M	1.00000	22	43	YY	8	4	1	0	0	0	3
71-11	7	M	1.00000	22	44	YY	7	6	1	0	0	0	4
71-11	7	M	1.00000	23	45	YY	5	11	0	0	0	0	10
71-11	7	M	1.00000	23	46	YY	6	9	2	0	0	0	5
71-11	7	M	1.00000	24	47	YY	4	6	0	0	0	0	6
71-11	7	M	1.00000	24	48	YY	8	2	0	0	0	0	7
71-11	7	M	1.00000	25	49	YY	5	10	0	0	0	0	14
71-11	7	M	1.00000	25	50	YY	0	1	0	2	0	0	5
71-11	7	M	1.00000	26	51	YY	6	8	0	1	0	0	6
71-11	7	M	1.00000	26	52	YY	7	7	0	0	0	0	12
71-11	7	M	1.00000	27	53	YY	0	6	0	0	0	1	7
71-11	7	M	1.00000	27	54	YY	8	3	0	0	0	0	6
71-11	7	M	1.00000	28	55	YY	2	9	0	0	0	0	8
71-11	7	M	1.00000	28	56	YY	6	8	0	0	0	0	9
71-11	7	M	1.00000	29	57	YY	6	9	1	0	0	0	6
71-11	7	M	1.00000	29	58	YY	7	4	0	0	0	0	6
71-11	7	M	1.00000	30	59	YY	4	5	0	0	0	0	7
71-11	7	M	1.00000	30	60	YY	7	4	0	0	0	0	5

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SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA		
							L	R	L	R	L	R	
71-11	7	M 5.00000	31	61	Y	6	8	2	2	0	0	7	8
71-11	7	M 5.00000	31	62	Y	5	5	2	0	0	0	5	5
71-11	7	M 5.00000	32	63	Y	5	8	0	0	0	0	5	8
71-11	7	M 5.00000	32	64	Y	5	8	0	0	0	0	5	8
71-11	7	M 5.00000	33	65	Y	5	6	0	1	0	0	7	6
71-11	7	M 5.00000	33	66	Y	8	7	0	0	0	0	9	7
71-11	7	M 5.00000	34	67	Y	9	5	0	0	0	0	9	5
71-11	7	M 5.00000	34	68	Y	10	5	0	0	0	0	10	5
71-11	7	M 5.00000	35	69	Y	4	7	0	0	0	0	5	8
71-11	7	M 5.00000	35	70	Y	5	7	0	0	0	1	5	7
71-11	7	M 5.00000	36	71	Y	6	4	0	0	0	0	10	6
71-11	7	M 5.00000	36	72	Y	5	10	0	0	0	0	5	10
71-11	7	M 5.00000	37	73	Y	8	6	1	1	0	0	8	6
71-11	7	M 5.00000	37	74	Y	8	2	1	0	0	0	10	2
71-11	7	M 5.00000	38	75	Y	9	5	1	0	0	0	9	5
71-11	7	M 5.00000	38	76	Y	6	8	0	0	0	0	6	8
71-11	7	M 5.00000	39	77	Y	6	2	0	0	0	0	6	4
71-11	7	M 5.00000	39	78	Y	7	6	3	1	0	0	8	6
71-11	7	M 5.00000	40	79	Y	5	6	0	0	0	0	5	6
71-11	7	M 5.00000	40	80	Y	7	6	0	0	0	0	7	6

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	R	L	H
CONTROL	8	S 0.00000	1	1	Y	4	6	0	0	0	0	5
CONTROL	8	S 0.00000	1	2	Y	6	8	0	4	0	0	6
CONTROL	A	S 0.00000	2	3	Y	8	3	0	0	0	0	8
CONTROL	8	S 0.00000	2	4	Y	9	3	0	0	1	0	9
CONTROL	A	S 0.00000	3	5	Y	6	7	0	0	0	0	6
CONTROL	8	S 0.00000	3	6	Y	6	7	0	0	0	0	6
CONTROL	A	S 0.00000	4	7	Y	5	8	0	2	0	0	5
CONTROL	A	S 0.00000	4	8	Y	4	9	0	1	0	0	4
CONTROL	8	S 0.00000	5	9	Y	7	6	1	3	0	0	7
CONTROL	8	S 0.00000	5	10	Y	11	2	2	0	0	0	12
CONTROL	A	S 0.00000	6	11	Y	4	7	0	0	0	0	4
CONTROL	8	S 0.00000	6	12	Y	6	5	0	0	0	0	6
CONTROL	8	S 0.00000	7	13	Y	10	1	0	0	0	0	10
CONTROL	A	S 0.00000	7	14	Y	3	10	0	0	0	0	3
CONTROL	8	S 0.00000	8	15	Y	6	8	0	0	0	1	6
CONTROL	8	S 0.00000	8	16	Y	5	7	0	0	0	0	6
CONTROL	A	S 0.00000	9	17	Y	8	7	1	0	0	0	8
CONTROL	A	S 0.00000	9	18	Y	7	7	1	0	0	0	7
CONTROL	8	S 0.00000	10	19	Y	3	7	0	0	0	0	3
CONTROL	8	S 0.00000	10	20	Y	8	5	4	2	0	0	8
71-11	8	S .20000	21	41	Y	9	5	0	0	0	0	9
71-11	8	S .20000	21	42	Y	5	6	0	0	0	0	6
71-11	8	S .20000	22	43	YY	7	4	0	0	0	0	7
71-11	A	S .20000	22	44	Y	5	6	1	1	0	0	5
71-11	8	S .20000	23	45	Y	8	8	0	0	0	0	8
71-11	8	S .20000	23	46	Y	8	6	0	0	0	0	6
71-11	8	S .20000	24	47	YY	7	8	0	1	0	0	7
71-11	8	S .20000	24	48	Y	8	4	0	1	0	0	8
71-11	A	S .20000	25	49	YY	7	7	2	1	0	0	7
71-11	8	S .20000	25	50	Y	5	8	1	1	1	0	6
71-11	A	S .20000	26	51	YY	5	2	0	0	0	0	8
71-11	A	S .20000	26	52	Y	5	7	0	0	0	0	5
71-11	8	S .20000	27	53	YY	7	4	0	0	0	0	8
71-11	8	S .20000	27	54	YY	6	5	0	1	0	0	7
71-11	A	S .20000	28	55	Y	6	5	0	0	0	0	6
71-11	8	S .20000	28	56	Y	4	7	0	3	0	1	4
71-11	A	S .20000	29	57	YY	6	6	0	0	1	0	6
71-11	8	S .20000	29	58	YY	7	6	0	0	1	0	7
71-11	8	S .20000	30	59	Y	3	7	0	0	0	0	6
71-11	8	S .20000	30	60	Y	9	4	0	0	1	0	10

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SODIUM SACCHARIN

PAGE 37

TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA		
								L	R	L	R	L	R	
71-11	8	S	1.00000	31	61	Y	3	8	0	0	0	0	3	10
71-11	8	S	1.00000	31	62	YY	4	9	0	0	0	0	4	9
71-11	8	S	1.00000	32	63	YY	5	7	0	0	0	0	6	7
71-11	8	S	1.00000	32	64	YY	6	7	1	0	0	0	6	7
71-11	8	S	1.00000	33	65	YY	6	6	0	0	0	0	6	6
71-11	8	S	1.00000	33	66	YY	11	4	0	0	0	0	11	4
71-11	8	S	1.00000	34	67	YY	7	6	1	0	0	0	8	6
71-11	8	S	1.00000	34	68	YY	10	7	0	0	0	0	10	7
71-11	8	S	1.00000	35	69	YY	7	4	0	0	0	0	8	4
71-11	8	S	1.00000	35	70	YY	4	9	0	0	0	0	5	9
71-11	8	S	1.00000	36	71	YY	5	9	1	0	0	0	5	10
71-11	8	S	1.00000	36	72	YY	6	9	0	1	1	1	6	11
71-11	8	S	1.00000	37	73	YY	8	8	1	1	1	0	10	11
71-11	8	S	1.00000	37	74	YY	9	4	0	0	0	0	9	5
71-11	8	S	1.00000	38	75	YY	5	9	3	0	0	0	6	12
71-11	8	S	1.00000	38	76	YY	1	1	1	1	0	0	6	5
71-11	8	S	1.00000	39	77	YY	8	5	0	0	0	0	8	6
71-11	8	S	1.00000	39	78	YY	7	8	0	2	0	0	7	8
71-11	8	S	1.00000	40	79	YY	4	7	0	0	0	0	4	7
71-11	8	S	1.00000	40	80	Y	6	7	0	0	0	0	6	7
71-11	8	S	5.00000	41	81	YY	7	7	0	0	0	0	7	7
71-11	8	S	5.00000	41	82	YY	8	6	0	0	0	0	9	7
71-11	8	S	5.00000	42	83	YY	10	7	1	0	0	1	10	7
71-11	8	S	5.00000	42	84	YY	0	7	0	0	0	0	4	8
71-11	8	S	5.00000	43	85	YY	3	9	0	3	0	0	3	9
71-11	8	S	5.00000	43	86	YY	10	3	0	0	1	0	10	4
71-11	8	S	5.00000	44	87	YY	8	8	1	0	0	0	8	8
71-11	8	S	5.00000	44	88	YY	7	8	6	1	0	1	7	8
71-11	8	S	5.00000	45	89	YY	6	6	0	0	0	0	6	6
71-11	8	S	5.00000	45	90	YY	8	5	0	0	0	0	8	5
71-11	8	S	5.00000	46	91	YY	11	5	1	0	0	0	12	5
71-11	8	S	5.00000	46	92	YY	0	8	0	0	0	0	4	8
71-11	8	S	5.00000	47	93	YY	7	5	1	0	0	1	8	5
71-11	8	S	5.00000	47	94	YY	7	8	0	0	0	0	7	8
71-11	8	S	5.00000	48	95	YY	7	3	0	0	0	1	8	4
71-11	8	S	5.00000	48	96	YY	6	7	0	0	0	0	8	8
71-11	8	S	5.00000	49	97	YY	4	9	0	0	0	0	4	9
71-11	8	S	5.00000	49	98	YY	5	7	0	0	0	0	8	7
71-11	8	S	5.00000	50	99	YY	7	7	0	0	0	0	7	8
71-11	8	S	5.00000	50	100	Y	10	5	0	0	0	0	11	5

DOMINANT LETHAL STUDY OF COMPOUND 71-11

SODIUM SACCHARIN

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	R	L	R	L	R
TEM	8	S	.00020	11	21	Y	6	10	0	0	0	0	8	10
TEM	8	S	.00020	11	22	Y	9	5	0	1	1	0	9	7
TEM	8	S	.00020	12	23	Y	4	9	1	1	0	0	6	9
TEM	8	S	.00020	12	24	Y	4	5	2	0	0	3	6	5
TEM	8	S	.00020	13	25	Y	6	5	0	0	1	1	6	5
TEM	8	S	.00020	13	26	Y	4	9	1	0	0	0	4	9
TEM	8	S	.00020	14	27	Y	9	5	0	0	0	0	9	6
TEM	8	S	.00020	14	28	Y	7	4	0	0	0	0	7	4
TEM	8	S	.00020	15	29	Y	6	4	0	0	0	0	6	4
TEM	8	S	.00020	15	30	Y	7	6	0	1	0	0	7	6
TEM	8	S	.00020	16	31	Y	8	3	0	0	0	0	8	4
TEM	8	S	.00020	16	32	Y	5	8	0	0	0	0	6	9
TEM	8	S	.00020	17	33	Y	7	3	0	0	0	1	7	4
TEM	8	S	.00020	17	34	Y	6	7	0	0	0	0	6	7
TEM	8	S	.00020	18	35	Y	5	8	0	0	0	0	5	8
TEM	8	S	.00020	18	36	Y	3	8	0	0	0	0	3	9
TEM	8	S	.00020	19	37	Y	8	5	0	1	0	0	8	6
TEM	8	S	.00020	19	38	Y	5	9	2	0	0	0	8	5
TEM	8	S	.00020	20	39	Y	8	5	0	0	0	0	9	3
TEM	8	S	.00020	20	40	Y	9	3	0	0	0	0	9	3

ARMITAGE TEST FOR A LINEAR TREND IN PROPORTIONS FOR THE FERTILITY INDEX
 (1 DEGREE OF FREEDOM) BASED ON THE DOSE LEVELS

	200 MG/KG		1 G/KG		5 G/KG		CHISQ (C-1)	CHISQ (1)	ARMTG CHISQ
WEEK	N	N	N	N	N	PRG MTD			
---	PRG	MTD	---	PRG	MTD	---	---	---	---
SINGLE TREATMENT									
1	16	20	18	20	20	20	4.44	3.87	.57
2	19	20	19	20	20	20	1.03	1.01	.03
3	20	20	20	20	20	20	0.00	0.00	0.00
4	20	20	19	20	20	20	2.03	.26	1.77
5	20	20	20	20	20	20	0.00	0.00	0.00
6	20	20	17	20	18	20	3.05	.35	2.70
7	20	20	20	20	19	20	2.03	1.98	.05
8	20	20	20	20	20	20	0.00	0.00	0.00
MULTIPLE TREATMENT									
1	19	20	14	20	16	20	4.23	.30	3.93
2	20	20	20	20	20	20	0.00	0.00	0.00
3	20	20	20	20	20	20	0.00	0.00	0.00
4	20	20	20	20	18	20	4.14	4.04	.10
5	18	20	16	20	20	20	4.44	2.69	1.76
6	20	20	20	20	19	20	2.03	1.98	.05
7	20	20	20	20	20	20	0.00	0.00	0.00

ARMITAGE TEST FOR A LINEAR TREND IN PROPORTIONS FOR THE FERTILITY INDEX
 (1 DEGREE OF FREEDOM) BASED ON THE LOGARITHMS OF THE DOSE LEVELS

WEEK	200 MG/KG		1 G/KG		5 G/KG		CHISQ (C-1)	CHISQ (1)	ARMTG CHISQ
	N	N	N	N	PRG	MTD			
	PRG	MTD	PRG	MTD	PRG	MTD			
SINGLE TREATMENT									
1	16	20	18	20	20	20	4.44	4.44	.00
2	19	20	19	20	20	20	1.03	.78	.26
3	20	20	20	20	20	20	0.00	0.00	0.00
4	20	20	19	20	20	20	2.03	.00	2.03
5	20	20	20	20	20	20	0.00	0.00	0.00
6	20	20	17	20	18	20	3.05	1.31	1.75
7	20	20	20	20	19	20	2.03	1.53	.51
8	20	20	20	20	20	20	0.00	0.00	0.00
MULTIPLE TREATMENT									
1	19	20	14	20	16	20	4.23	1.50	2.73
2	20	20	20	20	20	20	0.00	0.00	0.00
3	20	20	20	20	20	20	0.00	0.00	0.00
4	20	20	20	20	18	20	4.14	3.10	1.03
5	18	20	16	20	20	20	4.44	1.11	3.33
6	20	20	20	20	19	20	2.03	1.53	.51
7	20	20	20	20	20	20	0.00	0.00	0.00

**ARMITAGE TEST FOR A LINEAR TREND IN PROPORTIONS FOR THE FERTILITY INDEX
(2 DEGREES OF FREEDOM) BASED ON THE DOSE LEVELS AND INCLUDING THE CONTROL GROUP**

WEEK	CONTROL			200 MG/KG			1 G/KG			5 G/KG		
	N	N	N	N	N	N	N	N	CHISQ	CHISQ	ARMTG	CHISQ
	PRG	MTD	PRG	MTD	PRG	MTD	PRG	MTD	(C-1)	(1)	CHISQ	
SINGLE TREATMENT												
1	15	20	16	20	18	20	20	20	6.22	5.21	1.01	
2	20	20	19	20	19	20	20	20	2.05	.45	1.60	
3	20	20	20	20	20	20	20	20	0.00	0.00	0.00	
4	20	20	20	20	19	20	20	20	3.04	.07	2.96	
5	20	20	20	20	20	20	20	20	0.00	0.00	0.00	
6	20	20	20	20	17	20	18	20	5.76	1.43	4.33	
7	20	20	20	20	20	20	19	20	3.04	2.93	.10	
8	20	20	20	20	20	20	20	20	0.00	0.00	0.00	
MULTIPLE TREATMENT												
1	20	20	19	20	14	20	16	20	9.59	2.15	7.44	
2	20	20	20	20	20	20	20	20	0.00	0.00	0.00	
3	20	20	20	20	20	20	20	20	0.00	0.00	0.00	
4	20	20	20	20	20	20	18	20	6.15	5.94	.21	
5	18	20	18	20	16	20	20	20	4.44	2.16	2.28	
6	20	20	20	20	20	20	19	20	3.04	2.93	.10	
7	20	20	20	20	20	20	20	20	0.00	0.00	0.00	

DOMINANT LETHAL STUDY OF COMPOUND 71-11

SODIUM SACCHARIN

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T-TEST OF THE NUMBER OF IMPLANTATIONS IN PREGNANT FEMALES

WEEK	CONTROL		71-11 200 MG/KG				71-11 1 G/KG				71-11 5 G/KG				TEM		.2 MG/KG										
	N	PHG	STD	N	PRG	MEAN	STD	OF	T	N	PRG	MEAN	STD	OF	T	N	PHG	MEAN	STD	OF	T	N	PRG	MEAN	STD	OF	T
SINGLE TREATMENT																											
1	15	11.80	3.51	16	11.62	2.06	29		.171	18	11.94	1.76	31		.153	20	12.45	1.50	33		.745	17	11.82	1.51	30		
2	20	10.70	2.08	19	12.11	2.96	37		1.722	19	11.89	2.28	37		1.710	20	11.70	3.48	38		1.103	20	10.10	2.05	38		
3	20	12.25	1.71	20	11.90	2.95	38		.458	20	12.35	2.01	38		.169	20	12.25	1.21	38		0.000	20	7.35	3.20	38		
4	20	11.85	2.54	20	11.80	2.28	38		.065	19	11.42	1.84	37		.602	20	12.75	1.86	38		1.279	17	6.06	3.33	35		
5	20	12.30	3.42	20	12.80	3.09	38		.485	20	12.85	1.42	38		.664	20	14.00	1.30	38		2.079	20	11.30	2.43	38		
6	20	11.50	1.93	20	12.20	3.00	38		.877	17	11.94	2.16	35		.655	18	11.28	4.10	36		.217	20	12.65	1.63	38		
7	20	11.30	4.49	20	12.40	1.70	38		1.026	20	11.35	3.56	38		.039	19	12.63	1.26	37		1.248	20	13.05	1.57	38		
8	20	12.45	1.39	20	12.10	2.00	38		.643	20	12.80	3.02	38		.471	20	13.20	2.57	38		1.148	20	12.35	1.69	38		
MULTIPLE TREATMENT																											
1	20	11.15	2.68	19	11.53	2.55	37		.449	14	12.21	1.93	32		1.271	16	11.37	2.06	34		.276						
2	20	12.45	1.50	20	11.75	1.77	38		1.346	20	12.55	1.76	38		.193	20	10.45	3.98	38		2.102						
3	20	11.75	2.88	20	11.60	3.80	38		.141	20	12.10	2.55	38		.407	20	12.25	1.62	38		.677						
4	20	12.40	4.33	20	13.10	2.29	38		.639	20	13.10	3.23	38		.579	18	13.50	2.60	36		.936						
5	18	11.89	4.44	18	13.06	1.70	34		1.040	16	12.19	2.34	32		.240	20	11.90	1.89	36		.010						
6	20	12.20	1.85	20	11.50	2.69	38		.960	20	12.35	2.08	38		.241	19	13.00	1.86	37		1.347						
7	20	11.85	3.05	20	12.15	2.25	38		.354	20	11.70	3.39	38		.147	20	12.50	2.01	38		.796						

REGRESSION FITS OF THE NUMBER, U, OF IMPLANTATIONS ON 1) DOSE, AND 2) LOG DOSE
(PREDICTED U = A + BX)
CONTROL GROUP EXCLUDED

WEEK	X	N	XBAR	SD X	UBAR	SD U	B	A	TB	DF	VARU X	CV U	VARH	VARA	VARUHAN
SINGLE TREATMENT															
1	DOSE	54	2.24	2.16	12.04	1.77	.155	11.688	1.391	52	3.0764	.1457	.0125	.1196	.0570
	LOG DOSE	54	.12	1.32	12.04	1.77	.258	12.006	1.418	52	3.0721	.1456	.0332	.0574	.0569
2	DOSE	58	2.12	2.13	11.90	2.91	-.073	12.051	-.400	56	8.6072	.2466	.0331	.2469	.1464
	LOG DOSE	58	.03	1.33	11.90	2.91	-.126	11.900	-.431	56	8.6032	.2466	.0852	.1484	.1483
3	DOSE	60	2.07	2.12	12.17	2.15	.041	12.081	.310	58	4.6876	.1780	.0177	.1538	.0781
	LOG DOSE	60	.00	1.33	12.17	2.15	.109	12.167	.512	58	4.6743	.1777	.0451	.0779	.0779
4	DOSE	59	2.08	2.13	12.00	2.05	.240	11.500	1.944	57	4.0146	.1670	.0152	.1343	.0680
	LOG DOSE	59	.00	1.34	12.00	2.05	.295	12.000	1.480	57	4.1224	.1692	.0398	.0699	.0699
5	DOSE	60	2.07	2.12	13.22	2.14	.262	12.675	2.045	58	4.3450	.1577	.0164	.1426	.0724
	LOG DOSE	60	.00	1.33	13.22	2.14	.373	13.217	1.807	58	4.4101	.1589	.0426	.0735	.0735
6	DOSE	55	2.02	2.12	11.82	3.16	-.185	12.191	-.910	53	10.0353	.2680	.0412	.3501	.1825
	LOG DOSE	55	-.06	1.35	11.82	3.16	-.284	11.802	-.890	53	10.0421	.2681	.1022	.1829	.1826
7	DOSE	59	2.02	2.10	12.12	2.43	.135	11.847	.886	57	5.9214	.2008	.0232	.1945	.1004
	LOG DOSE	59	-.03	1.32	12.12	2.43	.066	12.120	.269	57	5.9953	.2020	.0594	.1017	.1016
8	DOSE	60	2.07	2.12	12.70	2.56	.188	12.312	1.196	58	6.5052	.2008	.0246	.2135	.1084
	LOG DOSE	60	.00	1.33	12.70	2.56	.342	12.700	1.369	58	6.4569	.2001	.0623	.1076	.1076
MULTIPLE TREATMENTS															
1	DOSE	49	2.00	2.14	11.67	2.21	-.077	11.827	-.511	47	4.9677	.1909	.0226	.1915	.1014
	LOG DOSE	49	-.10	1.37	11.67	2.21	-.035	11.670	-.150	47	4.9928	.1914	.0554	.1024	.1019
2	DOSE	60	2.07	2.12	11.58	2.81	-.353	12.312	-.2104	58	7.4423	.2355	.0281	.2442	.1240
	LOG DOSE	60	.00	1.33	11.58	2.81	-.404	11.583	-.1480	58	7.7187	.2398	.0745	.1266	.1286
3	DOSE	60	2.07	2.12	11.98	2.77	.104	11.769	.606	58	7.7609	.2325	.0293	.2547	.1293
	LOG DOSE	60	.00	1.33	11.98	2.77	.202	11.983	.739	58	7.7372	.2321	.0747	.1290	.1290
4	DOSE	58	1.97	2.08	13.22	2.70	.089	13.050	.513	56	7.3598	.2051	.0248	.2421	.1269
	LOG DOSE	58	-.06	1.31	13.22	2.70	.122	13.231	.446	56	7.3683	.2053	.0750	.1273	.1270
5	DOSE	54	2.21	2.18	12.37	2.00	-.189	12.788	-.1512	52	3.9160	.1600	.0156	.1488	.0725
	LOG DOSE	54	.06	1.36	12.37	2.00	-.356	12.392	-.1800	52	3.8487	.1586	.0392	.0714	.0713
6	DOSE	59	2.02	2.10	12.27	2.29	.265	11.737	1.891	57	5.0128	.1825	.0196	.1647	.0850
	LOG DOSE	59	-.03	1.32	12.27	2.29	.467	12.284	2.109	57	4.9418	.1812	.0489	.0838	.0838
7	DOSE	60	2.07	2.12	12.12	2.60	.114	11.881	.710	58	6.8060	.2153	.0257	.2233	.1134
	LOG DOSE	60	.00	1.33	12.12	2.60	.109	12.117	.423	58	6.8441	.2159	.0661	.1141	.1141

REGRESSION FITS OF THE NUMBER, U, OF IMPLANTATIONS ON DOSE
(PREDICTED U = A + B*x)
CONTROL GROUP INCLUDED

WEEK	X	N	XBAR	SD X	UBAR	SD U	B	A	TB	DF	VAMU X	CV U	VARM	VAMA	VARUBAR
SINGLE TREATMENT															
1	DOSE	69	1.76	2.12	11.99	2.23	.146	11.730	1.144	67	4.9626	.1859	.0162	.1220	.0719
2	DOSE	78	1.57	2.06	11.59	2.76	.058	11.499	.374	76	7.7078	.2395	.0236	.1573	.0988
3	DOSE	80	1.55	2.04	12.19	2.04	.025	12.148	.225	78	4.2048	.1683	.0128	.0893	.0526
4	DOSE	79	1.56	2.05	11.96	2.17	.207	11.640	1.750	77	4.5825	.1790	.0140	.0918	.0580
5	DOSE	80	1.55	2.04	12.99	2.53	.297	12.526	2.183	78	6.1014	.1902	.0186	.1209	.0763
6	DOSE	75	1.48	2.03	11.73	2.88	-.117	11.907	-.708	73	8.3355	.2461	.0275	.1713	.1111
7	DOSE	79	1.51	2.01	11.91	3.07	.187	11.630	1.085	77	9.3939	.2573	.0297	.1662	.1189
8	DOSE	80	1.55	2.04	12.64	2.32	.175	12.367	1.372	78	5.3138	.1824	.0162	.1053	.0664
MULTIPLE TREATMENTS															
1	DOSE	69	1.42	2.02	11.52	2.35	-.007	11.532	-.052	67	5.6000	.2054	.0203	.1219	.0812
2	DOSE	80	1.55	2.04	11.80	2.56	-.366	12.367	-2.687	78	6.0876	.2091	.0185	.1206	.0761
3	DOSE	80	1.55	2.04	11.92	2.78	.106	11.761	.686	78	7.7934	.2341	.0237	.1544	.0974
4	DOSE	78	1.46	1.99	13.01	3.18	.151	12.792	.825	76	10.1849	.2452	.0335	.2021	.1306
5	DOSE	72	1.66	2.12	12.25	2.79	-.104	12.423	-.063	70	7.8294	.2284	.0246	.1767	.1087
6	DOSE	79	1.51	2.01	12.25	2.17	.221	11.921	1.833	77	4.5911	.1749	.0145	.0910	.0581
7	DOSE	80	1.55	2.04	12.05	2.70	.117	11.869	.783	78	7.3245	.2246	.0223	.1451	.0916

T-TEST OF THE (TRANSFORMED) PRE-IMPLANTATION LOSSES IN PREGNANT FEMALES
 (LOSSES TAKEN AS A SUBSET OF CORPORA LUTEA)

WEEK	CONTROL				71-11 200 MG/KG				71-11 1 G/KG				71-11 5 G/KG				1&M .2 MG/KG						
	N PRG	MEAN	STD DEV	STU DF	N PRG	MEAN	STD DEV	DF	N PRG	MEAN	STD DEV	DF	T	N PRG	MEAN	STD DEV	DF	T	N PRG	MEAN	STD LEV DF	T	
SINGLE TREATMENT																							
1	15	.52	.59	16	.62	.36	29	.568	18	.50	.28	31	.137	20	.46	.26	33	.425	17	.64	.36	30	.704
2	20	.72	.38	19	.67	.46	37	.368	19	.70	.37	37	.138	20	.62	.60	38	.640	20	.95	.32	38	2.089
3	20	.46	.25	20	.61	.50	38	1.228	20	.54	.33	38	.870	20	.48	.24	38	.241	20	1.20	.59	38	5.196
4	20	.68	.35	20	.55	.40	38	.630	19	.55	.29	37	.739	20	.47	.27	38	.060	17	1.57	.48	35	7.941
5	20	.63	.54	20	.45	.49	38	1.089	20	.46	.22	38	1.279	20	.52	.27	38	.751	20	.58	.43	38	.314
6	20	.58	.33	20	.67	.48	38	.704	17	.41	.29	35	1.666	18	.71	.68	36	.721	20	.46	.25	38	1.389
7	20	.74	.68	20	.52	.34	38	1.331	20	.67	.58	38	.378	19	.37	.26	37	2.293	20	.48	.25	38	1.654
8	20	.44	.21	20	.60	.30	38	1.941	20	.63	.45	38	1.665	20	.55	.36	38	1.183	20	.56	.29	38	1.499
MULTIPLE TREATMENT																							
1	20	.66	.49	19	.58	.45	37	.553	14	.51	.39	32	.973	16	.57	.34	34	.638					
2	20	.50	.30	20	.61	.26	38	1.251	20	.59	.33	38	.871	20	.81	.72	38	1.751					
3	20	.57	.46	20	.67	.57	38	.623	20	.51	.42	38	.467	20	.47	.23	38	.851					
4	20	.77	.60	20	.59	.37	38	1.171	20	.53	.47	38	1.423	18	.47	.36	36	1.869					
5	18	.80	.66	18	.66	.32	34	.795	16	.65	.49	32	.741	20	.65	.31	36	.949					
6	20	.53	.38	20	.59	.51	38	.434	20	.52	.33	38	.049	19	.44	.25	37	.858					
7	20	.61	.44	20	.57	.41	38	.336	20	.71	.60	38	.567	20	.50	.33	38	.914					

T-TEST OF THE NUMBER OF DEAD IMPLANTS

WEEK	CONTROL				71-11 200 MG/KG				71-11 1 G/KG				71-11 5 G/KG				TEM .2 MG/KG						
	N	PRG	STD	N	PRG	STD	N	PRG	STD	N	PRG	STD	N	PRG	STD	N	PRG	STD	N	PRG			
SINGLE TREATMENT																							
1	15	.40	.83	16	.63	1.26	29	.584	18	.28	.57	31	.499	20	.70	1.38	33	.746	17	3.24	2.63	30	3.991
2	20	.40	.75	19	.84	1.38	37	1.247	19	.74	1.10	37	1.122	20	.75	1.25	38	1.071	20	6.65	4.18	38	6.575
3	20	.80	1.47	20	.60	.60	38	.563	20	.60	.68	38	.551	20	.45	.69	38	.963	20	5.45	3.28	38	6.399
4	20	.45	.60	20	1.15	1.50	38	1.939	19	.79	1.62	37	.876	20	1.30	2.03	38	1.796	17	5.41	2.74	35	7.894
5	20	1.20	1.44	20	.90	1.52	38	.642	20	.55	.76	38	1.789	20	.60	.88	38	1.592	20	3.00	2.08	38	3.187
6	20	.75	.85	20	.90	.85	38	.557	17	.88	1.27	35	.378	18	1.33	1.88	36	1.254	20	.35	.67	38	1.651
7	20	.35	.49	20	.35	.49	38	0.000	20	.35	.59	38	0.000	19	.37	.60	37	.106	20	.70	.92	38	1.498
8	20	1.15	1.69	20	.85	1.23	38	.642	20	.75	1.07	38	.893	20	1.00	1.86	38	.266	20	.90	1.25	38	.531
MULTIPLE TREATMENT																							
1	20	1.75	1.77	19	.74	.73	37	2.309	14	1.29	1.98	32	.717	16	.63	.89	34	2.313					
2	20	1.10	1.25	20	.95	1.23	38	.381	20	.40	.60	38	2.256	20	1.05	1.36	38	.121					
3	20	.90	1.41	20	.45	.69	38	1.283	20	.55	.89	38	.939	20	1.05	1.36	38	.343					
4	20	1.45	1.76	20	.40	.68	38	2.487	20	.80	1.15	38	1.381	18	.89	1.45	36	1.065					
5	18	.83	1.47	18	.78	1.52	34	.112	16	.75	1.06	32	.188	20	.60	1.20	36	.077					
6	20	.50	.89	20	.70	1.17	38	.607	20	1.00	1.75	38	1.141	19	1.16	1.46	37	1.707					
7	20	1.05	1.36	20	.75	1.62	38	.635	20	.55	.69	38	1.471	20	.80	1.28	38	.599					

ARMITAGE TEST FOR A LINEAR TREND IN PROPORTIONS FOR THE DEATH INDEX
 (1 DEGREE OF FREEDOM)
 BASED ON THE DOSE LEVELS

	200 MG/KG		1 G/KG		5 G/KG				
WEEK	N WDI	N PRG	N WDI	N PRG	N WDI	N PRG	CHISQ (C-1)	CHISQ (1)	ARMTG CHISQ
----	---	---	---	---	---	---	-----	-----	-----
SINGLE TREATMENT									
1	6	16	4	18	8	20	1.53	.42	1.10
2	10	19	8	19	8	20	.71	.40	.32
3	11	20	10	20	7	20	1.74	1.73	.01
4	11	20	8	19	13	20	2.06	1.10	.96
5	7	20	8	20	8	20	.14	.06	.09
6	13	20	7	17	11	18	2.37	.07	2.30
7	7	20	6	20	6	19	.12	.02	.10
8	9	20	8	20	9	20	.14	.02	.12
MULTIPLE TREATMENT									
1	11	19	6	14	7	16	.99	.40	.59
2	10	20	7	20	10	20	1.21	.16	1.06
3	7	20	7	20	12	20	3.39	3.31	.08
4	6	20	11	20	9	18	2.81	.61	2.20
5	7	18	8	16	8	20	.52	.04	.48
6	9	20	7	20	11	19	2.06	1.37	.69
7	7	20	9	20	8	20	.42	.01	.41

AMMITSAGE TEST FOR A LINEAR TREND IN PROPORTIONS FOR THE DEATH INDEX
(1 DEGREE OF FREEDOM).
BASED ON THE LOGARITHMS OF THE DOSE LEVELS

	200 MG/KG		1 G/KG		5 G/KG				
WEEK	N WDI	N PRG	N WDI	N PRG	N WDI	N PRG	CHISQ (C-1)	CHISO (1)	ARMTG CHISO
SINGLE TREATMENT									
1	6	16	4	18	8	20	1.53	.06	1.47
2	10	19	8	19	8	20	.71	.62	.09
3	11	20	10	20	7	20	1.74	1.61	.13
4	11	20	8	19	13	20	2.06	.40	1.66
5	7	20	8	20	8	20	.14	.11	.04
6	13	20	7	17	11	18	2.37	.08	2.28
7	7	20	6	20	6	19	.12	.05	.07
8	9	20	8	20	9	20	.14	.00	.14

MULTIPLE TREATMENT

1	11	19	6	14	7	16	.99	.74	.25
2	10	20	7	20	10	20	1.21	.00	1.21
3	7	20	7	20	12	20	3.39	2.55	.85
4	6	20	11	20	9	18	2.81	1.62	1.19
5	7	18	8	16	8	20	.52	.00	.51
6	9	20	7	20	11	19	2.06	.62	1.44
7	7	20	9	20	8	20	.42	.10	.31

ARMITAGE TEST FOR A LINEAR TREND IN PROPORTIONS FOR THE DEATH INDEX
 (2 DEGREES OF FREEDOM) BASED ON THE DOSE LEVELS AND INCLUDING THE CONTROL GROUP

WEEK	CONTROL		200 MG/KG		1 G/KG		5 G/KG					
	N	N	N	N	N	N	WDI	PRG	WDI	PRG	WDI	PRG
	WDI	PRG	WDI	PRG	WDI	PRG	(C-1)	(1)	CHISQ	ARMTG	CHISQ	
SINGLE TREATMENT.												
1	4	15	6	16	4	18	8	20	1.80	.65	1.15	
2	5	20	10	19	8	19	8	20	3.18	.02	3.16	
3	7	20	11	20	10	20	7	20	2.59	.61	1.98	
4	8	20	11	20	8	19	13	20	3.26	2.03	1.23	
5	11	20	7	20	8	20	8	20	1.84	.14	1.71	
6	11	20	13	20	7	17	11	18	2.37	.08	2.29	
7	7	20	7	20	6	20	6	19	.17	.04	.13	
8	10	20	9	20	8	20	9	20	.40	.01	.39	

MULTIPLE TREATMENT												
1	15	20	11	19	6	14	7	16	4.92	2.15	2.77	
2	13	20	10	20	7	20	10	20	3.60	.11	3.49	
3	8	20	7	20	7	20	12	20	3.48	3.07	.41	
4	12	20	6	20	11	20	9	18	4.15	.04	4.12	
5	8	18	7	18	8	16	8	20	.53	.06	.48	
6	6	20	9	20	7	20	11	19	3.63	2.58	1.05	
7	9	20	7	20	9	20	8	20	.57	.01	.56	

DOMINANT LETHAL STUDY OF COMPOUND 71-11

SODIUM SACCHARIN

PAGE 50

PROBIT ANALYSIS OF THE PROPORTION OF PREGNANT FEMALES WITH ONE OR MORE DEAD IMPLANTS
 $\text{PROBIT} = A + B(\text{LOG DOSE})$

WEEK	B	A	CHISQ	DF
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SINGLE TREATMENT

1	.072	4.565	1.47	1
2	-.228	4.872	.09	1
3	-.364	4.914	.14	1
4	.182	5.107	1.67	1
5	.094	4.703	.04	1
6	-.084	5.158	2.29	1
7	-.069	4.537	.06	1
8	-.000	4.832	.14	1

MULTIPLE TREATMENT

1	-.262	4.963	.25	1
2	-.000	4.874	1.21	1
3	.460	4.827	.82	1
4	.377	4.875	1.23	1
5	.014	4.813	.51	1
6	.227	4.896	1.44	1
7	.093	4.746	.31	1

T-TEST OF THE (TRANSFORMED) NUMBER OF DEAD IMPLANTS
 (DEAD IMPLANTS TAKEN AS A SUBSET OF IMPLANTS)

WEEK	CONTROL				71-11 200 MG/KG				71-11 1 G/KG				71-11 5 G/KG				TEM 10 MG/KG						
	N	PRG	MEAN	STD DEV	N	PRG	MEAN	STD DEV	DF	T	N	PRG	MEAN	STD DEV	DF	T	N	PRG	MEAN	STD DEV	DF	T	
SINGLE TREATMENT																							
1	15	.44	.24	16	.50	.35	.29	.582	18	.38	.20	31	.689	.20	.50	.36	33	.549	17	1.05	.55	30	3.970
2	20	.45	.28	19	.62	.54	.37	1.265	19	.51	.28	37	.690	.20	.54	.33	38	.902	20	1.97	.48	38	6.674
3	20	.51	.38	20	.53	.23	.38	.207	20	.50	.23	38	.156	.20	.44	.23	38	.746	20	2.27	.72	38	9.643
4	20	.46	.20	20	.63	.37	.38	1.836	19	.53	.36	37	.812	.20	.63	.37	38	1.848	17	2.53	.36	35	22.037
5	20	.63	.34	20	.53	.35	.38	.995	20	.46	.25	38	1.803	.20	.45	.27	38	1.849	20	1.09	.54	38	3.212
6	20	.57	.30	20	.62	.31	.38	.531	17	.55	.36	35	.149	.18	.78	.57	36	1.452	20	.40	.22	38	2.067
7	20	.53	.47	20	.42	.19	.38	1.013	20	.47	.35	38	.427	.19	.41	.21	37	1.016	20	.51	.27	38	.203
8	20	.59	.37	20	.54	.33	.38	.404	20	.57	.53	38	.130	.20	.54	.37	38	.365	20	.57	.36	38	.160
MULTIPLE TREATMENT																							
1	20	.86	.58	19	.59	.34	.37	1.776	14	.60	.43	32	1.423	.16	.52	.32	34	2.096					
2	20	.63	.32	20	.59	.36	.38	.331	20	.42	.21	38	2.377	.20	.77	.66	38	.853					
3	20	.56	.36	20	.53	.48	.38	.202	20	.48	.33	38	.698	.20	.61	.33	38	.454					
4	20	.72	.41	20	.41	.21	.38	3.042	20	.54	.28	38	1.642	.18	.59	.58	36	.809					
5	18	.58	.39	18	.49	.35	.34	.699	16	.54	.31	32	.341	.20	.52	.31	36	.517					
6	20	.43	.24	20	.54	.31	.38	1.138	20	.54	.39	38	.979	.19	.60	.33	37	1.757					
7	20	.67	.58	20	.50	.37	.38	1.087	20	.57	.48	38	.593	.20	.51	.33	38	1.029					

CONTROL GROUP ANOVA FOR THE NUMBER OF PREGNANT FEMALES

WEEK	BETWEEN MALES			WITHIN MALES			TOTAL			F
	SUMSQ	DF	MEANSD	SUMSQ	DF	MEANSD	SUMSQ	DF		
SINGLE TREATMENT										
1	1.250	9	.139	2.500	10	.250	3.750	19		.556
2	0.000	9	0.000	0.000	10	0.000	0.000	19		I
3	0.000	9	0.000	0.000	10	0.000	0.000	19		I
4	0.000	9	0.000	0.000	10	0.000	0.000	19		I
5	0.000	9	0.000	0.000	10	0.000	0.000	19		I
6	0.000	9	0.000	0.000	10	0.000	0.000	19		I
7	0.000	9	0.000	0.000	10	0.000	0.000	19		I
8	0.000	9	0.000	0.000	10	0.000	0.000	19		I
MULTIPLE TREATMENT										
1	0.000	9	0.000	0.000	10	0.000	0.000	19		I
2	0.000	9	0.000	0.000	10	0.000	0.000	19		I
3	0.000	9	0.000	0.000	10	0.000	0.000	19		I
4	0.000	9	0.000	0.000	10	0.000	0.000	19		I
5	1.600	9	.200	0.000	10	0.000	1.600	19		H
6	0.000	9	0.000	0.000	10	0.000	0.000	19		I
7	0.000	9	0.000	0.000	10	0.000	0.000	19		I

CONTROL GROUP ANOVA FOR THE NUMBER OF IMPLANTATIONS PER PREGNANT FEMALE

WEEK	BETWEEN MALES			WITHIN MALES			TOTAL			F
	SUMSQ	DF	MEANSQ	SUMSQ	DF	MEANSQ	SUMSQ	DF		
SINGLE TREATMENT										
1	123.600	9	13.756	51.000	5	10.200	174.800	14		1.349
2	42.200	9	4.689	40.000	10	4.000	82.200	19		1.172
3	26.250	9	2.917	29.500	10	2.950	55.750	19		.989
4	59.050	9	6.561	63.500	10	6.350	122.550	19		1.033
5	75.200	9	8.356	147.000	10	14.700	222.200	19		.568
6	39.000	9	4.333	32.000	10	3.200	71.000	19		1.354
7	175.200	9	19.467	207.000	10	20.700	382.200	19		.940
8	19.450	9	2.161	17.500	10	1.750	36.950	19		1.235
MULTIPLE TREATMENT										
1	71.050	9	7.894	65.500	10	6.550	136.550	19		1.205
2	24.450	9	2.717	18.500	10	1.850	42.950	19		1.468
3	63.250	9	7.028	94.500	10	9.450	157.750	19		.744
4	251.000	9	27.978	105.000	10	10.500	356.800	19		2.665
5	132.778	8	16.597	203.000	9	22.556	335.778	17		.736
6	25.200	9	2.800	40.000	10	4.000	65.200	19		.700
7	57.050	9	6.339	119.500	10	11.950	176.550	19		.530

CONTROL GROUP ANOVA FOR THE PRE-IMPLANTATION LOSS PER PREGNANT FEMALE

WEEK	BETWEEN MALES			WITHIN MALES			TOTAL			F
	SUMSQ	DF	MEANSQ	SUMSQ	DF	MEANSQ	SUMSQ	DF		
SINGLE TREATMENT										
1	71.550	9	7.950	65.000	5	13.000	136.550	14	.612	
2	24.450	9	2.717	28.500	10	2.850	52.950	19	.953	
3	7.450	9	.828	5.500	10	.550	12.950	19	1.505	
4	12.050	9	1.339	18.500	10	1.850	30.550	19	.724	
5	42.600	9	4.756	72.000	10	7.200	114.800	19	.660	
6	14.000	9	1.556	14.000	10	1.400	28.000	19	1.111	
7	86.200	9	9.578	95.000	10	9.500	181.200	19	1.008	
8	1.450	9	.161	5.500	10	.550	6.950	19	.293	
MULTIPLE TREATMENT										
1	43.450	9	4.828	75.500	10	7.550	118.950	19	.639	
2	24.200	9	2.689	21.000	10	2.100	45.200	19	1.280	
3	25.450	9	2.828	45.500	10	4.550	70.950	19	.621	
4	89.800	9	9.978	115.000	10	11.500	204.800	19	.868	
5	123.444	8	15.431	101.000	9	11.222	224.444	17	1.375	
6	38.800	9	4.311	37.000	10	3.700	75.800	19	1.165	
7	30.050	9	3.339	32.500	10	3.250	62.550	19	1.027	

CONTROL GROUP ANOVA FOR THE NUMBER OF DEAD IMPLANTS PER PREGNANT FEMALE

WEEK	BETWEEN MALES			WITHIN MALES			TOTAL			F
	SUMSQ	DF	MEANSQ	SUMSQ	DF	MEANSQ	SUMSQ	DF		
SINGLE TREATMENT										
1	9.437	9	1.049	.500	5	.100	9.937	14		10.486
2	7.600	9	.867	3.000	10	.300	10.800	19		2.889
3	18.200	9	2.022	23.000	10	2.300	41.200	19		.879
4	3.450	9	.383	3.500	10	.350	6.950	19		1.095
5	20.200	9	2.222	19.000	10	1.900	39.200	19		1.181
6	6.250	9	.694	7.500	10	.750	13.750	19		.926
7	2.050	9	.228	2.500	10	.250	4.550	19		.911
8	25.050	9	2.783	29.500	10	2.950	54.550	19		.944
MULTIPLE TREATMENT										
1	38.250	9	4.250	21.500	10	2.150	59.750	19		1.977
2	17.800	9	1.978	12.000	10	1.200	29.800	19		1.648
3	22.800	9	2.533	15.000	10	1.500	37.800	19		1.689
4	15.450	9	1.717	43.500	10	4.350	58.950	19		.395
5	12.000	8	1.500	24.500	9	2.722	36.500	17		.651
6	5.000	9	.556	10.000	10	1.000	15.000	19		.556
7	10.450	9	1.161	24.500	10	2.450	34.950	19		.474

CONTROL GROUP ANOVA FOR THE RATIO OF DEAD IMPLANTS TO TOTAL IMPLANTS PER PREGNANT FEMALE

WEEK	BETWEEN MALES			WITHIN MALES			TOTAL		
	SUMSU	DF	MEANSQ	SUMSU	DF	MEANSQ	SUMSQ	DF	F
SINGLE TREATMENT									
1	.045	9	.005	.003	5	.001	.048	14	8.413
2	.093	9	.010	.031	10	.003	.124	19	3.297
3	.147	9	.016	.185	10	.019	.332	19	.883
4	.020	9	.002	.022	10	.002	.042	19	1.001
5	.129	9	.014	.100	10	.010	.229	19	1.434
6	.069	9	.008	.091	10	.009	.159	19	.839
7	.416	9	.046	.514	10	.051	.929	19	.899
8	.146	9	.016	.168	10	.017	.314	19	.964
MULTIPLE TREATMENT									
1	.627	9	.070	.526	10	.053	1.153	19	1.323
2	.122	9	.014	.088	10	.009	.211	19	1.536
3	.163	9	.018	.087	10	.009	.250	19	2.093
4	.147	9	.016	.220	10	.022	.367	19	.742
5	.125	8	.016	.240	9	.027	.365	17	.584
6	.628	9	.003	.055	10	.006	.083	19	.564
7	.504	9	.056	.564	10	.056	1.069	19	.993

T-TEST OF THE NUMBER OF CORPORA LUTEA IN PREGNANT FEMALES

WEEK	CONTROL				71-11 200 MG/KG				71-11 1 G/KG				71-11 5 G/KG				TFM .2 MG/KG							
	N PHG	MEAN	STD DEV	N PHG	MEAN	STD DEV	DF	T	N PHG	MEAN	STD DEV	DF	T	N PHG	MEAN	STD DEV	DF	T	N PHG	MEAN	STD DEV	DF	T	
SINGLE TREATMENT																								
1	15	12.93	1.71	16	12.87	1.75	29	.094	18	12.67	1.75	31	.441	20	13.15	1.40	33	.348	17	13.29	1.57	30	.622	
2	20	12.75	1.33	19	13.63	2.24	37	2.354	19	13.68	2.81	37	2.054	20	13.45	2.21	38	2.078	20	12.75	1.83	38	.987	
3	20	12.80	1.64	20	13.15	1.31	38	.746	20	13.25	1.33	38	.952	20	12.85	1.31	38	.107	20	11.05	1.93	38	3.087	
4	20	12.50	2.04	20	12.80	1.47	38	.533	19	12.37	2.50	37	.181	20	13.40	1.73	36	1.506	17	12.06	2.36	35	.611	
5	20	13.70	1.63	20	13.55	1.54	38	.300	20	13.40	1.39	38	.627	20	15.00	1.65	38	2.507	20	12.50	1.88	38	2.161	
6	20	12.50	1.54	20	13.95	1.70	38	2.827	17	12.35	1.69	35	.277	18	13.06	1.70	36	1.059	20	13.25	1.80	38	1.415	
7	20	13.10	2.36	20	13.50	2.59	38	.511	20	12.95	1.76	38	.228	19	12.95	1.43	37	.243	20	13.70	1.38	38	.982	
8	20	12.90	1.29	20	13.15	1.69	38	.524	20	14.25	2.47	38	2.166	20	14.25	1.77	38	2.750	20	13.45	2.67	38	.830	
MULTIPLE TREATMENT																								
1	20	12.70	1.59	19	12.68	1.29	37	.034	14	13.14	.77	32	.961	16	12.31	1.74	34	.696						
2	20	13.25	1.25	20	12.75	1.52	38	1.137	20	13.75	1.52	38	1.137	20	13.20	2.14	38	.090						
3	20	12.80	1.36	20	13.45	3.41	38	.792	20	13.20	2.24	38	.683	20	12.85	1.84	38	.098						
4	20	14.80	3.62	20	14.55	2.74	38	.246	20	14.20	1.54	38	.682	18	14.28	1.71	36	.558						
5	18	14.33	1.91	18	14.72	2.27	34	.556	16	14.38	3.76	32	.041	20	13.25	2.15	36	1.635						
6	20	13.30	1.81	20	12.75	1.12	38	1.156	20	13.20	1.40	38	.196	19	13.58	1.98	37	.460						
7	20	13.00	2.08	20	13.35	1.66	38	.588	20	13.85	2.91	38	1.064	20	13.35	1.73	36	.580						